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Pathology

EXPERIMENTAL PATHOLOGY

1. A Study of the Pathogenesis of Rheumatic-like Lesions in the Guinea Pig

R. S. JONES and Y. CARTER. *Archives of Pathology* [*Arch. Path.* (*Chicago*)] **58**, 613–635, Dec., 1954. 30 figs., 47 refs.

This lengthy study from the University of Oregon Medical School, Portland, is concerned with the changes produced in the cardiac valves and the joints of guinea-pigs by injection of various chemicals and organisms. Some of these produced proliferative changes, but the changes were not regarded as specific. The authors, while admitting that no specific thesis has been proved, hope that these experiments will widen the horizon for future investigation. *A. C. Lendrum*

2. Rheumatic-like Lesions in the Guinea-pig: a Correlation of Toxic, Anaphylactogenic, Arthropathic and Chemical Properties of Certain Crude Polysaccharides from *Klebsiella pneumoniae* Type B

R. S. JONES, Y. CARTER, and J. DE W. RANKIN. *British Journal of Experimental Pathology* [*Brit. J. exp. Path.*] **35**, 519–527, Dec., 1954. 7 figs., 20 refs.

In previous studies [not yet published] the two first-named authors found that certain mucopolysaccharides obtained from gastric mucin and a Friedländer type of organism produced lesions of the cardiac valves and joints on injection into guinea-pigs. In the investigations here reported from the University of Oregon Medical School, Portland, mucopolysaccharide fractions prepared from agar cultures of *Klebsiella pneumoniae* Type B were injected into guinea-pigs. Chemical analysis showed much variation in the protein nitrogen, hexosamine, and hexuronic acid content of different batches of the material used. Studies were made of the toxicity of these substances following intravenous injection, and of their ability to induce anaphylactic hypersensitivity by subcutaneous injection. [It is not possible from the description given to form a clear idea of how the experiments were carried out.]

Active anaphylaxis was induced in guinea-pigs by only one of the fractions—an " acid-hydrolysis " fraction prepared by Wong's method (*Proc. Soc. exp. Biol.* (*N.Y.*), 1938, **38**, 107 and 110), and this was also shown to be toxic. An " alkaline-hydrolysis " fraction was non-anaphylactigenic and less toxic. Daily injections of 2·5 or 5 mg. (intravenously or subcutaneously) of either fraction resulted in the development of cardiac valve lesions and synovial proliferative changes, with exudate, in certain joints, both reactions occurring within 1 to 14 days of the first injection. The authors regard the cardiac changes as non-specific and as part of a general inflammatory response in the guinea-pig, but consider that the changes in the joints are more specifically related to the injection of mucopolysaccharides. *E. J. Holborow*

CHEMICAL PATHOLOGY

3. Determination of the Hepatic Blood Flow by Galactose

A. T. HANSEN, N. TYGSTRUP, and K. WINKLER. *Danish Medical Bulletin* [*Dan. med. Bull.*] **1**, 146–149, Oct., 1954. 1 fig., 14 refs.

Hepatic blood flow can be determined according to the Fick principle by giving a single intravenous injection of galactose and making serial measurements of the galactose concentration in blood from the brachial artery and a catheterized hepatic vein. The rate at which galactose is removed by the liver is independent of its concentration in the blood over a wide range. In 4 subjects studied at the University Hospital, Copenhagen, hepatic blood flow was measured simultaneously by this method and by the " bromsulphalein " clearance method, and there was good agreement between the results given by the two techniques. The galactose method is unsuitable for measuring changes in hepatic blood flow of short duration, and a correction has to be made for urinary excretion of galactose, but it may be more reliable than the bromsulphalein method in patients with liver damage, in whom the excretion of bromsulphalein is greatly reduced. *P. C. Reynell*

4. Copper Sulfate as Reagent in Cerebrospinal Fluid Analysis

C. DE CHENAR. *Texas Reports on Biology and Medicine* [*Tex. Rep. Biol. Med.*] **12**, 453–463, 1954.

The purpose of this work has been to find an appropriate chemical compound for a sufficiently sensitive globulin reaction of the cerebrospinal fluid which reaction, to a certain extent, may be regarded as an approximate quantitative test indicating the grades of alteration during the course of observation. As a theoretical support of the experimentations, the colloid-chemical properties of the cerebrospinal fluid were outlined.

Experiments with animals were carried out and the reaction was used in comparison with other globulin reactions in more than 2,300 cases of routine cerebrospinal fluid examination and of 19 organic diseases affecting the central nervous system. The reagent is a 0·05% solution of chemically pure $CuSO_4.5H_2O$ in triple distilled water. 0·5 ml. of this reagent is pipetted into three small test tubes, and 0·25 ml. of the spinal fluid is added to the first one, 0·5 ml. to the second, and 0·75 ml. to the third one. The proportion of the spinal fluid to the reagent is 1 : 2, 1 : 1, and 3 : 2.

When no pathological alteration is present, an opalescence in the third test tube results. In cases of pathological changes with an increased globulin percentage opalescence or precipitation in heavier form results in the second and first test tubes, depending on the amount of the globulin, particularly gamma globulin, in the contents. In this manner, it is possible to draw certain conclusions as to the quantitative correlation of the case. The application of this reaction succeeded in finding nuances in the globulin proportion, and the reaction was positive in several cases where other globulin reactions did not give a definite result and where the anamnesis and clinical findings were concordant with its positiveness. This is a simple and time-saving reaction. —[Author's summary.]

HAEMATOLOGY

5. Rapid Rh-typing. A "Sandwich" Technique

F. STRATTON. *British Medical Journal* [*Brit. med. J.*] **1**, 201–203, Jan. 22, 1955. 1 fig., 4 refs.

This paper from the Manchester Regional Blood Transfusion Service and the University of Manchester describes a technique for the rapid Rh-typing of blood before transfusion, the whole procedure occupying little more than 10 minutes. It is emphasized that this method is not intended to be used for routine typing of large numbers of specimens.

Equal quantities (approximately 0·03 ml.) of bovine albumin, anti-Rh serum, and a suspension of washed erythrocytes are placed on a slide and mixed with the edge of a second slide as in making a blood film. The second slide is then lowered on to the first and the resulting "sandwich" is incubated for 10 minutes at 37° C. A control in which Group-AB serum is substituted for anti-Rh serum is also set up. The slides are then examined under the low power of the microscope, when clumping will be observed if the reaction is positive.

The author examined by this technique 1,000 blood samples which had been separated into D-positive (including D^u-positive) and D-negative groups by routine tube-agglutination methods. There was complete correlation between the two techniques in the detection of 149 specimens of D-negative blood. Of the 851 specimens classed as D-positive by tube agglutination, 847 were also D-positive by the new technique, while in 2 the reaction was negative and in 2 doubtful. The doubtful and negative reactions all occurred with D^u-positive blood, which is known not to be detected by the albumin technique. No false positive results were obtained. Apart from its rapidity, this method has the advantage over other slide-agglutination techniques that it is not necessary to use especially avid Rh-typing sera.

Nigel Compston

6. A Simple Method of Rh-typing

P. W. HARVEY. *British Medical Journal* [*Brit. med. J.*] **1**, 203–205, Jan. 22, 1955. 1 fig., 4 refs.

From Ancoats Hospital, Manchester, the author reports a new rapid method for Rh-typing suitable for use before transfusion. The technique has been developed from a modification of the method described by Poole and Williams (*J. clin. Path.*, 1951, **4**, 55), in which agglutination tubes are first incubated at 37° C. for 7 to 15 minutes and then centrifuged at about 500 r.p.m.; the tubes are then tapped to resuspend the cells and both incubation and centrifuging repeated. The "thermal centrifuging method" here described employs a specially designed lagged centrifuge incorporating a thermostatically controlled heating element. Centrifuging (at 100 to 150 r.p.m.) and incubation can therefore be performed at the same time.

The results obtained after 15, 20, and 30 minutes' centrifuging were compared with those obtained with a variety of other methods in a total of 249 cases. The thermal centrifuging method gave no false negative results, and with a centrifuging time of 20 minutes weak positive results (such as inexperienced workers may find difficult to read) were reduced to a minimum.

Nigel Compston

7. The Clotting Action of Russell Viper Venom

S. I. RAPAPORT, K. AAS, and P. A. OWREN. *Blood* [*Blood*] **9**, 1185–1194, Dec., 1954. 24 refs.

The authors present observations which explain the differences between the "thromboplastic" activity of Russell viper venom and that of brain thromboplastins. These differences include: (1) the failure of venom to accelerate the clotting of plasma from which all platelet and lipid material has been removed; (2) the rapid clotting time of 4 to 8 seconds obtained with venom–lipid combinations compared with 12 to 15 seconds with most tissue thromboplastins; and (3) the failure of prothrombin-time determinations to measure the full effect of dicoumarol administration when venom is substituted for brain thromboplastin.

In experiments carried out at the University Hospital, Oslo, the authors showed that Russell viper venom in the presence of lipid co-factor can clot the plasma of patients with haemophilia and haemophilia B and plasma deficient in proconvertin within 5 seconds. It is, however, unable to clot proaccelerin-deficient plasma rapidly, so that the clotting behaviour of venom–lipid combinations is similar to that of convertin. They suggest a rapid presumptive test for hypoproconvertinaemia, consisting in the estimation of the clotting time by Quick's method first with brain thromboplastin and then with Russell viper venom. With proconvertin-deficient plasma the former gives a prolonged thromboplastin time and the latter a normal thromboplastin time.

With prothrombin-deficient or proaccelerin-deficient plasma both agents will give a prolonged clotting time.

The special characteristics of Russell viper venom are thus explained by its ability to act independently of the proconvertin content of plasma. *Janet Vaughan*

MORBID ANATOMY AND CYTOLOGY

8. Cerebral Shrinking

K. G. JAMIESON. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] 3, 312–317, Nov., 1954. 2 figs., 4 refs.

Unlike cerebral swelling and oedema, shrinking of the brain has hitherto received little consideration. Generalized shrinking may be caused by vasoconstriction or cerebral dehydration; localized shrinking, which is discussed in this paper from Alfred Hospital, Melbourne, is the result of a space-occupying lesion.

Space-occupying lesions usually enlarge slowly and produce at first only a slight rise in intracranial pressure limited to the cranio-septal compartment in which the lesion is situated. This rise in pressure, insufficient to impede capillary circulation, is transmitted to the tissue fluid and, in the absence of other decisive osmotic and hydrostatic pressure changes, tends to retard the formation and to accelerate the absorption of tissue fluid. The resulting hydrostatic balance is precarious; if the rise in pressure exceeds a critical level, venous compression sets in and is followed by oedema or swelling of the brain. As the lesion expands, pressure is transmitted to other cranio-septal compartments, initiating similar changes there.

The progressive shrinking of the brain and the fluctuation between shrinking and venous congestion are reflected in the clinical signs and symptoms in many conditions. Treatment, which must be directed towards preventing the venous pressure from exceeding a critical level, includes nursing in the erect position, avoidance of respiratory obstruction and of general anaesthesia, and, whenever possible, the direct elimination of the cause of venous obstruction. *L. Crome*

9. The Pathology of Infectious Mononucleosis. (Zur Pathologie der Mononucleosis infectiosa)

W. WERNER. *Virchows Archiv für pathologische Anatomie und Physiologie und für klinische Medizin* [*Virchows Arch. path. Anat.*] **326**, 155–171, 1954. 12 figs., bibliography.

In this communication from the University Institute of Pathology, Leipzig, the author discusses the pathology of infectious mononucleosis, with special reference to a fatal case in a boy of 17 who died on the 11th day of illness from oedema of the glottis; this case had been tentatively diagnosed as faucial diphtheria. Post-mortem examination showed widespread lymphadenopathy, hepato-splenomegaly, oedema of the lungs, and congestion in many organs. The Paul–Bunnell reaction was positive (1 in 32). The histological findings are given in great detail: there was infiltration of the lymph-node sinusoids with reticulum cells and lymphoid cells of varying degrees of maturity; the spleen, which weighed 730 g., had a congested pulp, with focal accumulation of lymphoid and monocytoid elements, as well as reactive centres in the Malpighian corpuscles, while the bone marrow was hyperplastic and also contained foci of lymphoid cells.

A study of 24 fatal cases reported in the literature showed that the main causes of death in infectious mononucleosis are rupture of the spleen (10 cases), ascending paralysis of the Landry–Guillain–Barré type (4), oedema of the glottis (2), and peritonsillar abscess (2). In a further 12 cases with rupture of the spleen prompt surgical intervention saved the patient's life. The earliest change in the lymph nodes and spleen is enlargement of the follicles due to increase in the number of reticulum cells and of lymphocytes in the sinuses; later the demarcation between the two becomes more indistinct. In the spleen the architecture is obscured by a dense and diffuse infiltration by lymphoid and lymphatic elements. The pathogenesis is further discussed in detail as it affects the bone marrow, lungs, heart, gastrointestinal mucosa, pancreas, liver, and skin. In patients dying with neurological symptoms necropsy reveals petechial perivascular haemorrhages (haemorrhagic encephalomyelopathy) and loose mononuclear infiltration of the leptomeninges and of the anterior spinal roots. Hyperplasia of lympho-reticular tissue and focal interstitial perivascular lymphatic and lymphoid infiltration of most tissues are the main features.

The mortality as quoted in the literature ranges from 0·1 to 1%. In patients who recover, complete regression of the lesions may possibly take years, but no permanent changes have been reported. In differentiating the condition from leukaemia the almost universal recovery and a blood picture showing a 50 to 90% relative mononucleosis with the appearance of abnormal lymphoid cells are important points. Acute septicaemia should also be borne in mind. The author concludes that infectious mononucleosis is an inflammatory reticulo-endothelial reaction to the presence of a virus.

F. Hillman

10. Infantile Progressive Muscular Atrophy. Value of Muscle Biopsy in the Diagnosis of and Its Differentiation from Muscular Dystrophy

H. S. ROSENBERG and A. J. MCADAMS. *Archives of Pathology* [*Arch. Path. (Chicago)*] **58**, 604–612, Dec., 1954. 5 figs., 10 refs.

The value of muscle biopsy in the diagnosis of infantile progressive muscular atrophy was studied at the Children's Medical Center and Harvard Medical School, Boston. Material obtained at necropsy in 23 cases in which progressive muscular atrophy, muscular dystrophy, or atrophy of poliomyelitis had been diagnosed was examined to determine the presence or absence of changes in the central nervous system. The histological appearances of specimens of muscle from these cases and of similar specimens taken at biopsy were then studied. In most of the cases in which muscle disease was secondary to changes in the central nervous system there was a patchy distribution of irregular-sized muscle fibres, whereas in cases without central or peripheral

nervous system involvement diffuse intermingling of fibres of all sizes was observed.

On the basis of these findings the authors attempted to correlate the histological appearances of muscle biopsy specimens with the clinical diagnosis, and found that such correlation existed in all but 3 out of 19 cases —namely, 2 cases of amyotonia congenita in which diffuse intermingling of fibres was seen and one case of muscular dystrophy in which there was patchy distribution of the affected muscle bundles.

The presence or absence of sarcolemmal nuclear proliferation, fatty infiltration, muscle-cell degeneration, and myophagia was of little help in diagnosis.

J. B. Enticknap

11. **Intralobar Bronchopulmonary Sequestration Studied by Multicolored Vinyl Acetate Cast: Report of Case**

M. L. LEMMON, J. W. KIRKLIN, and M. B. DOCKERTY. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **29**, 631–637, Dec. 8, 1954. 3 figs., 14 refs.

The authors report the discovery at the Mayo Clinic of a case of intralobar broncho-pulmonary sequestration with an anomalous artery to the lung in a healthy young woman of 22 who was undergoing routine radiological examination. The anomaly, which has often been described, consists of a mass of ectopic lung or maldeveloped broncho-pulmonary cystic tissue supplied by a large elastic artery arising from the descending aorta in the region of the pulmonary ligament.

In the present case the right lower lobe of the lung, which was found to contain numerous congenital cysts in its posterior basal segment, was removed at exploratory thoracotomy and the vasculature studied after injection of red, blue, and yellow vinyl acetate into the anomalous artery and the pulmonary artery and vein respectively. The vessels and their branches were found to be coarser than in normal lung. There were no anastomoses in this case with the normal pulmonary artery. As described by Pryce *et al.* (*Brit. J. Surg.*, 1947, **35**, 18; *Abstracts of World Surgery*, 1948, **3**, 121) the venous drainage was into the pulmonary vein.

D. M. Pryce

12. **Pathology of the Pulmonary Vascular Tree. IV. Structural Changes in the Pulmonary Vessels in Chronic Left Ventricular Failure**

R. C. SMITH, H. B. BURCHELL, and J. E. EDWARDS. *Circulation* [*Circulation (N.Y.)*] **10**, 801–808, Dec., 1954. 1 fig., 12 refs.

In a study carried out at the Mayo Clinic the authors have attempted to assess quantitatively the histological changes in the pulmonary vessels in chronic left ventricular failure. Two groups of cases were investigated: (1) those in which there was manifest failure due to calcific aortic stenosis or systemic hypertension (24 cases), and (2) a similar group in which, however, failure was not manifest (24 cases); specimens from a third group of 20 patients dying from conditions other than cardiac disease were examined as a control. The muscular arteries, arterioles, and veins in at least two post-mortem specimens of the lung from each subject were studied, and alterations in them were expressed as an "index of change", this index being the product of an arbitrary "grade of severity" and a "grade of distribution" obtained by averaging the appearances in the two sections. The results for the three groups were compared with each other (and afterwards with the average indices of change in the same pulmonary vascular elements in 10 cases of mitral stenosis).

It was clear that the changes in the arteries, arterioles, and veins in Group 1 were quite different from those in the other two groups, but notably similar to those in the cases of mitral stenosis. The most marked differences from the control group (Group 3) occurred in the media of the muscular arteries in Groups 1 and 2, the changes in the intima being not so obvious. It was noted that 8 of the cases in Group 2 showed a greater index of change than those of Group 1. This may have been because in these cases failure had been present although not manifest, or alternatively it may have been the result of a response to left ventricular failure—the so-called "protective" contraction of the small arteries which helps to prevent the occurrence of pulmonary oedema.

E. G. Rees

13. **Cancer Metastases in the Spleen**

R. I. S. DUNN. *Glasgow Medical Journal* [*Glasg. med. J.*] **36**, 43–49, Feb., 1955. 6 figs., 13 refs.

14. **Latent Carcinoma of the Prostate**

L. M. FRANKS. *Journal of Pathology and Bacteriology* [*J. Path. Bact.*] **68**, 603–616, 1954. 31 figs., 25 refs.

The Registrar-General's returns for England and Wales for 1952 showed that 1·38% of all deaths in males over 50 years of age were due to carcinoma of the prostate. In the United States the reported incidence of prostatic carcinoma in men over the age of 50 has varied from 14 to 46%. In an attempt to assess the true incidence of this disease the author, at the Royal College of Surgeons, London, examined the prostate of 220 males of all ages on whom necropsy had been performed because death was sudden or unexpected. Carcinoma of the prostate was found in 69 cases; all the affected subjects were 50 or more years of age, giving a percentage incidence of latent carcinoma of the prostate in this age group of 37.

The methods of examination used and the criteria of malignancy adopted are fully described. The diameter of the tumours varied from 0·1 to 5·8 cm. The small acinar type was commonest, usually beginning at the periphery of the prostate in a multicentric manner. In only 16 of the 69 cases was the tumour diagnosed macroscopically. Infiltration of the capsule, with local spread, was common; there was infiltration into vessels in 26 cases and into benign adenomata in 22. The author states that there is no evidence to suggest that malignancy of the prostate is related to benign hyperplasia; there is, however, an apparent connexion with oestrogen secretion.

W. Skyrme Rees

See also Tuberculosis, Abstract 50.

Microbiology and Parasitology

15. **A New Method for the Culture of Anaerobic Organisms.** (Nuovo metodo di coltura per germi anaerobi)
V. DEL VECCHIO. *Igiene e sanità pubblica* [*Igiene Sanit. pubbl.*] **10**, 225–229, May–June, 1954 [received Jan., 1955]. 3 figs., 3 refs.

The author describes a simple method for the culture of anaerobic organisms. The method is similar to that first described by Koch in 1884, but Koch used plain agar and mica slips and his method was not suitable for strict anaerobes. In the modified method here described liver–agar is used as the medium, on to which a broth culture of the organism is inoculated and evenly distributed. It is emphasized that the agar must have a perfectly flat surface to exclude as much air as possible. A sterile glass slide is then placed on the surface of the plate before incubation, when growth occurs under the slide only. In many cases if incubation is continued for 48 hours or longer gas formation disrupts the medium. It is claimed that sensitivity to antibiotics can also be determined by placing the antibiotic to be tested adjacent to the edge of the glass slide.

R. F. Jennison

16. **Further Studies Concerning a Receptor-destroying Factor in Human Saliva from Healthy Donors and from Poliomyelitis Patients**
C. W. JUNGEBLUT and A. W. KNOX. *Journal of Immunology, Virus Research and Experimental Chemotherapy* [*J. Immunol.*] **73**, 264–272, Nov., 1954. 1 fig., 6 refs.

In an earlier study the authors, with Horvath (*Arch. Pediat.*, 1952, **69**, 321), had shown that human saliva frequently possesses the property of rendering human erythrocytes insusceptible to the haemagglutinin of Columbia SK virus, and that when human Group-O erythrocytes were exposed to the action of the saliva of certain individuals they became " panagglutinable ", that is, agglutinable by human Group-AB serum. This power to render cells " panagglutinable " correlated absolutely with the power to render them insusceptible to the Columbia SK haemagglutinin. In the present study, at Columbia University, New York, the authors employed a technique based on the former property.

The unknown factor in human saliva has many of the characteristics of an enzyme and is not considered to be of bacterial origin, although it is apparently similar to the receptor-destroying enzyme of *Vibrio cholerae*. The factor is not found in the serum or cerebrospinal fluid. Saliva from healthy persons and from poliomyelitic patients in both the acute and convalescent stages of the disease was examined at intervals for this activity. While the proportion of individuals whose saliva was intermittently positive was similar in both groups, the saliva from the patients with poliomyelitis was significantly more frequently positive than that from the healthy controls. It is suggested that the presence of the receptor-destroying factor in saliva may be due to some environmental condition such as infection or virus carriage, or that it may be evidence of some constitutional susceptibility to poliomyelitis in the individual.

J. E. M. Whitehead

17. **A Receptor-destroying Enzyme in Human Saliva and its Possible Relation to Poliomyelitis Infection**
B. HOFMAN. *Journal of Immunology, Virus Research and Experimental Chemotherapy* [*J. Immunol.*] **73**, 273–277, Nov., 1954. 13 refs.

In a study of saliva from healthy persons, poliomyelitic patients, and patients with other diseases, carried out at the Netherlands Institute for Preventive Medicine, Leiden, the author observed that some samples of " negative " saliva had the power of neutralizing the activity of " positive " saliva, and that this neutralizing power was thermostable. It is considered that the secretion of the receptor-destroying factor in the saliva is probably a constitutional characteristic which varies with the individual, and that persons secreting the factor have a greater chance of becoming infected by poliomyelitis virus, possibly because saliva reacts with substances in the alimentary tract of a mucoid nature able to neutralize the virus.

[This paper from the Netherlands provides independent confirmation of the work of Jungeblut and Knox in most details (see Abstract 16).]

J. E. M. Whitehead

18. **Further Experience in the Preparation and Use of Complement-fixing Antigens for the Diagnosis of Mumps.** (Weitere Erfahrungen bei der Herstellung und Auswertung komplementbindender Antigene für die Diagnose der Mumpsinfektion)
F. MÜLLER and H. LIPPELT. *Zeitschrift für Hygiene und Infektionskrankheiten* [*Z. Hyg. InfektKr.*] **140**, 372–378, 1954. 8 refs.

In an investigation carried out at the Bernhard Nocht Institute, Hamburg, it was shown that the V antigen of mumps virus, prepared by the high-speed centrifugation of infected allantoic fluid after dialysis for 20 hours against Tyrode solution and re-suspended in allantoic fluid, retained its haemagglutinating and complement-fixing activity unaltered after 6 months' storage at −10° C., while the S antigen, extracted from the chorio-allantoic membrane of infected eggs and suspended in allantoic fluid, lost only a little complement-fixing power after a similar period of storage. The authors attribute the stability of the antigens to the use of allantoic fluid for suspension.

Dialysis of infected allantoic fluid against 10 volumes of glycerin for 12 hours at 4° C. gave a preparation containing 4 times as much V antigen as the centrifuged preparation and no detectable S antigen. The two V-antigen preparations had equal complement-fixing activity, but the haemagglutinating power of that prepared

with glycerin was 10% higher. The glycerin preparation was stable when stored for 6 months at −10° C.

Complement-fixation tests were carried out with both preparations on 100 unselected sera. Both preparations gave the same result in 86 cases, and the glycerin preparation gave a positive result in 12 additional cases in which the reaction with the centrifuged preparation was negative. There were 67 positive reactions, in 42 of which the glycerin preparation gave a higher titre than the centrifuged preparation and in 8 a lower titre. The method of dialysis against glycerin is therefore regarded as preferable to the centrifugation method in the preparation of V antigen for diagnostic purposes in mumps. *M. Lubran*

19. **Antibody Production with Isolated Bacterial Cell-walls and with Protoplasts.** (Antikörperproduktion mit isolierter Bakterienzellwand und mit Protoplasten)
J. Tomcsik and S. Guex-Holzer. *Experientia* [*Experientia* (*Basel*)] **10**, 484–485, Dec. 15, 1954. 2 figs., 6 refs.

A preparation containing the free, intact protoplasts of an anaerobic bacillus was obtained by lysozyme digestion of a suspension of the organism in isotonic saccharose solution. Ten intravenous injections of this preparation were given at 3-day intervals to rabbits, from whose blood an antiserum was then obtained which contained no polysaccharide antibody; it reacted with suspensions of protoplasts and of living bacilli, but not with suspensions of bacilli heated to 60° C. This thermolabile antigen on the cell surface was thought to be most probably a protein. Agglutinability of the organism by protoplast antiserum was greatly diminished by prolonged treatment with trypsin.

A substance obtained from the cell wall of the same organisms by treatment with trypsin was also used for immunizing rabbits. The resulting antiserum could be absorbed with polysaccharide derived from the capsule and cell wall and caused agglutination of both living and heated bacilli. It was responsible for most of the serological reactions of the cell surface. The agglutinability of the cells by this antiserum was unaffected by prolonged trypsinization. *M. Lubran*

20. **Bacteriophage Active against Virulent *Mycobacterium tuberculosis*. I. Isolation and Activity**
S. Froman, D. W. Will, and E. Bogen. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **44**, 1326–1333, Oct., 1954. 4 figs., 13 refs.

Spontaneous lysis of old cultures of human tubercle bacilli has been described and bacteriophages have been isolated which act on the saprophytic acid-fast bacilli. No reference has been found in the literature, however, to a bacteriophage which is active against human or bovine *Mycobacterium tuberculosis*. At the University of California, Los Angeles, the authors found that 4 out of 26 strains of bacteriophage examined attacked both *Myco. tuberculosis* and the saprophytic mycobacteria. All 4 were isolated from the soil by enrichment culture with saprophytic mycobacteria; enrichment culture with virulent tubercle bacilli did not yield any bacteriophage active against *Myco. tuberculosis*. Using either Petri dishes or 6- to 8-oz. (170- to 227-ml.) flat medicine bottles into which was poured a layer of Bordet–Gengou agar base with added peptone, the authors examined various mycobacteria for their susceptibility to bacteriophage action. The strain to be tested was grown in liquid Dubos' medium, and from this was seeded a tube of molten semisolid Bordet–Gengou agar base with added glycerol. The semisolid medium was layered on the first medium and dried. Bacteriophage suspensions were " spotted " on to the surface, the plates or bottle being then incubated at 37° C. and observed for plaque formation. Of 231 strains of human *Myco. tuberculosis*, 192 were susceptible to at least 2 of the 4 bacteriophages, as were 10 out of 12 strains of bovine *Myco. tuberculosis*, 3 out of 5 strains of B.C.G., and 115 out of 211 saprophytic strains. All of 14 strains of avian *Myco. tuberculosis* were resistant.

[The possible application of this work to the epidemiology of tuberculosis will depend on further study of the properties of these bacteriophages and standardization of the methods employed.] *J. E. M. Whitehead*

21. **Adenoidal–Pharyngeal–Conjunctival Agents. A Newly Recognized Group of Common Viruses of the Respiratory System**
R. J. Huebner, W. P. Rowe, T. G. Ward, R. H. Parrott, and J. A. Bell. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 1077–1086, Dec. 30, 1954. 2 figs., 12 refs.

Working at the U.S. National Microbiological Institute and Johns Hopkins University, the authors have been able to isolate, by means of tissue-culture techniques, 6 new viruses which, they consider, may be of importance as aetiological agents in a number of undifferentiated upper respiratory diseases. They propose that these 6 immunologically distinct types be given the generic name of " adenoidal–pharyngeal–conjunctival agents " to indicate the sites in which they are found.

The viruses were identified in cultures of adenoid and tonsillar tissue after prolonged incubation, it being presumed that they eventually outgrew their specific inhibitory antibodies, which were gradually washed out by the repeated changes of tissue-culture fluid. All 6 types are reported to grow readily and to produce unique cytopathogenic effects in human epithelial cells and HeLa cells *in vitro*, but they are non-pathogenic for laboratory animals. They are resistant to ether and antibodies, heat-labile, and filterable. They produce type-specific neutralizing antibodies and group-specific (but not type-specific) complement-fixing antibodies.

Serological surveys in the area of Washington, D.C., indicate that at one year 50% of infants have been infected with at least one of these agents and by the age of 15 the average person has been infected with several.

[This work, which is reminiscent of the discovery of the Coxsackie viruses, is an important milestone of progress in the study of respiratory infection and of virology in general. Further communications are promised, in which an attempt will presumably be made to define the precise clinical syndromes associated with these new agents.] *D. Geraint James*

Pharmacology

22. Deodorizing Experiments with Ion Exchange Resins

K. IKAI. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **23**, 411–422, Dec., 1954. 3 figs., 9 refs.

Previous work had convinced the author that the odour of axillary sweat and other cutaneous secretions is determined by their content of certain lower fatty acids, together with ammonia constituents, volatile salts (trimethylamine, methylamine), saturated ketones, and indole. Similarly, the factors responsible for the odour of faeces are said to be fatty acids, together with skatole, indole, methylmercaptan, hydrogen sulphide, and other substances. It seemed possible that these substances might be adsorbed by polyamine ion-exchange resins, and offensive odours removed in this way. A number of anion-exchange resins were therefore investigated at Nagoya City University Medical School, Japan, for their power of adsorption of fatty acids, cation-exchange resins being similarly tested for adsorption of ammonia, while both types were tested for the adsorption of indole, which is amphoteric. The degree of adsorption was determined by shaking up 0·05 to 0·5 g. of the resin with 10 ml. of the test solution and titrating the residual test substance in the supernatant fluid after a standard period of contact. Acetic acid and ammonia were used in M/10 concentration, the single-chain fatty acids from C_1 to C_6 in M/100 solution, and the much less soluble indole in M/1,000 solution. The residual indole after adsorption was determined colorimetrically after treatment of the supernatant fluid with sodium nitroprusside and sodium hydroxide. The results varied with the particular resin used, adsorption by some resins being almost complete and by others only about 40% under the same conditions. In the case of the fatty acids there was a direct correlation between the degree of adsorption by any particular resin and the dissociation constant of the acid. Deodorization and decolorization tests were then carried out, 1 g. of various resins being added, singly or in combination, to 10 ml. of urine or of a filtrate of faeces diluted 10 times and a rough estimate of the effect on the odour and colour being made by several observers. The results again varied with the different resins, a mixture of cation and anion exchangers (especially "amberlite" XE-98 and IR-4B) being the most effective. In similar experiments carried out with ether extracts of axillary sweat from osmidrotic subjects good results were obtained with the majority of resins investigated.

A number of pairs of ion-exchange resins were then tested by topical application to the axilla of osmidrotic subjects in a variety of vehicles at intervals of 12 hours, appraisal of the axillary odour being made at the beginning and end of each period. The powdered resins dusted thickly over the axillary skin abolished odour immediately upon application, but the effect was short-lived. With various ointments and emulsions in which the resins were incorporated in a strength of 20%, however, the deodorant effect lasted for 1 to 3 days in some cases. The most important characteristics of a vehicle for this purpose were found to be hydrophilia (to attract the sweat), non-ionization (so as not to interfere with the action of the resin), and good surface dispersion and penetration. *H. F. Reichenfeld*

23. Gastric and Intestinal Motility Studies with Morphine, Atropine, Hexamethonium Bromide and "Banthine"

R. ANDREW. *Australasian Annals of Medicine* [*Aust. Ann. Med.*] **3**, 305–311, Nov., 1954. 8 figs., 13 refs.

Gastric and intestinal motility was studied at the Baker Medical Research Institute and Alfred Hospital, Melbourne, by recording the pressure changes in balloons introduced into the pyloric antrum, the duodenal cap, and the proximal jejunum, the balloons being attached to a 4-lumen Miller–Abbott tube; the fourth channel served for the introduction of drugs into the stomach. The 12 subjects included 8 patients with active duodenal ulcer and 1 with gastric ulcer, and 3 healthy medical students. The behaviour of the normal gut is discussed and emphasis is laid on the great variability which may be observed in the same individual within a short space of time. The complexity of the recorded wave form and the speed with which one form of activity may change to another suggest that results obtained over a short interval are likely to be more informative than those of longer experiments. The changes produced by drugs are: (1) relative or absolute quiescence, or complete inhibition; and (2) augmentation of the waves or the production of tetany-like spasm with the occurrence of superimposed small waves at the rate of 9 to 12 per minute. A preliminary test in this investigation showed that the introduction of 200 ml. of normal saline by Miller–Abbott tube did not alter the motility of the stomach or upper small intestine.

In 2 of the patients with duodenal ulcer one-quarter grain (16 mg.) of morphine sulphate injected subcutaneously caused spasm of the duodenal cap and jejunum within 2 minutes of injection. This accords with the well-known constipating action of morphine by causing delayed intestinal propulsion. Atropine had a pronounced inhibitory action at all three sites when 1/100 grain (0·6 mg.) was given subcutaneously or intravenously to 2 patients, one with gastric and the other with duodenal ulcer, the action appearing within one minute. A dose of 1/200 of a grain (0·3 mg.) had no effect in a normal subject and produced only a transient partial loss of intestinal activity in the patient with gastric ulcer. Hexamethonium bromide (100 mg. given intramuscularly) was tested in one patient with duodenal ulcer; it took effect after one minute and caused complete inhibition for 85 minutes at all three sites. "Banthine" (methantheline bromide) was given

by stomach tube to 3 patients with ulcer and the 3 healthy controls. The effect of a dose of 100 mg. in 10 ml. of water varied from complete inhibition at all 3 sites to a partial effect on the duodenum and jejunum only. The action of the drug began after a delay of from 5 to 30 minutes and lasted for periods varying from 19 to 65 minutes.

The findings are discussed, particularly those produced by methantheline. It is considered that the therapeutic action of this drug in peptic ulceration may also involve depression of acid secretion. But on the whole no clear difference in the response of normal subjects and patients with peptic ulcer was apparent, and the author concludes that the effect of dose and individual variation of response are probably more important factors in this respect than the presence or absence of ulceration.

Derek R. Wood

24. **Comparison of Some Pharmacological Properties of Chlorpromazine, Promethazine, and Pethidine**
J. KOPERA and A. K. ARMITAGE. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] 9, 392–401, Dec., 1954. 8 figs., 39 refs.

In anaesthetic practice chlorpromazine is usually given in combination with promethazine and pethidine, so that it is difficult to judge the contribution made by each to the joint effect. The authors, working in the Department of Pharmacology, University of Oxford, have therefore made a quantitative and qualitative comparison of the pharmacological properties of the three drugs.

The results were as follows. All three drugs lowered the body temperature of the mouse, chlorpromazine being about 30 times as effective as the other two. Chlorpromazine was also the most effective depressant of muscular contraction when tested upon the gastrocnemius muscle of the cat and a phrenic-nerve–diaphragm preparation of the rat. Its action was not curare-like but directly upon the muscle, the response to both direct and indirect stimulation being abolished. The authors suggest that the lowering of body temperature produced by the drug may be the result of lowering of tonus, and therefore of heat-production, of skeletal muscles. Large doses of hexamethonium produced only a slight fall in body temperature, showing that the effect of chlorpromazine does not depend upon a ganglion-blocking action.

In a study of chronic toxicity it was found that young rats failed to grow during the first few days of continued administration of the drugs. The fact that pethidine produced not drowsiness but excitement may perhaps be an indication that it affected the metabolic rate. After a few days tolerance to all three drugs was acquired, and the test rats grew at the same rate as controls. Comparison of the doses required to retard growth showed that chlorpromazine was about five times as toxic as the other two drugs.

No potentiation was observed upon the analgesic effect of morphine, and of the three drugs only promethazine showed even an additive action. Chlorpromazine was much more effective than promethazine or pethidine in prolonging pentobarbitone anaesthesia in mice. Chlorpromazine was the most active antagonist of the action of adrenaline on the vessels of the rabbit ear, the blood pressure of the spinal cat, and the isolated rabbit uterus. It had very little antagonistic action against noradrenaline, and it is therefore suggested that noradrenaline could be used to restore the blood pressure in patients treated with chlorpromazine.

Anti-acetylcholine activity was tested on the isolated ileum of the guinea-pig, the mouse pupil, and salivary secretion in the cat. Promethazine was the most active of the three drugs; chlorpromazine was more active than pethidine on isolated gut, but showed no mydriatic activity at all. Chlorpromazine had about one-thirtieth of the inhibitory potency of atropine upon salivary secretion. All three drugs showed antihistaminic activity upon guinea-pig ileum and bronchioles, promethazine being the most potent and pethidine the weakest. The antihistaminic action was greater than the anti-acetylcholine action. Chlorpromazine exhibited the strongest and pethidine the weakest local analgesic effect when tested on intracutaneous weals in guinea-pigs.

It is concluded that in some respects chlorpromazine is more active than promethazine or pethidine, but that in general all three substances have the same type of pharmacological action. *L. G. Goodwin*

25. **The Pharmacological Properties of 2-Methyl-2-*n*-propyl-1:3-propanediol Dicarbamate (Miltown), a New Interneuronal Blocking Agent**
F. M. BERGER. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **112**, 413–423, Dec., 1954. 2 figs., 20 refs.

The author has investigated the pharmacological properties of a new interneuronal blocking agent designated " miltown " (2-methyl-2-*n*-propyl-1:3-propanediol dicarbamate) which produces a reversible flaccid paralysis of the skeletal muscles. This substance is one of a large series of compounds produced by blocking, with a carbamate group, the primary hydroxyl group present in mephenesin which is responsible for that drug's short duration of action. Miltown, which has very low solubility, is similar in action to mephenesin, and differs from the barbiturates in producing a slow, smooth induction without causing signs of hyperexcitability. The induction period for the mean paralytic dose in mice was 25 minutes for miltown and 2 minutes for mephenesin, but on the other hand the mean duration of action was 67 and 6 minutes respectively. Miltown is readily and rapidly absorbed from the gastrointestinal canal, and does not cause nausea or vomiting.

The drug was then tested on various animal species. Monkeys receiving 200 mg. per kg. body weight became more manageable within 30 minutes, showed no objection to being handled, no sign of fear, and readily accepted food. After about 60 minutes they became paralysed without showing any sign of excitement, and rested peacefully on their sides. In cats reflex activity was abolished after a longer latent period and for a more prolonged period than with mephenesin. Miltown was strikingly more effective than mephenesin in protecting mice from convulsions and death caused by

toxic doses of pentylenetetrazole. The mean dose required to prevent the extensor tonic phase of seizures produced by electric shock was 165 mg. per kg. for miltown and 415 mg. per kg. for mephenesin, and only transient protection was afforded by mephenesin. Miltown also prolonged the duration of barbiturate-induced sleep and prevented posthypnotic excitement.

In 4 dogs given 1 g. of miltown daily for 60 days haematological and renal function tests, as well as post-mortem examination, revealed no abnormality. In a test for chronic toxicity 3 groups of rats were fed with diets containing 0·5, 1, and 2% of miltown respectively for 15 months. The body weight of the animals receiving 2% of the drug was less than those in the control group, but those receiving 0·5% showed no significant difference. At the twelfth week 6 pairs from each group were mated; all the progeny were normal at birth, but those from parents receiving the 2% concentration of the drug died in the first week of life. All treated animals excreted small amounts of reducing agents in their urine, but the quantity of these agents did not increase throughout the study. Miltown in doses of 25 mg. per kg. body weight restored the body temperature to normal in rabbits rendered pyrexic with pyrogenic materials. It is concluded that miltown has all the properties of mephenesin and the additional great advantage of a duration of action nearly eight times as long.

Robert Hodgkinson

26. **Some Effects of N-Methyl-*alpha*-phenylsuccinimide (Milontin) on the Central Nervous System**

W. H. FUNDERBURK and R. T. WOODCOCK. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **112**, 404–412, Dec., 1954. 4 figs., 10 refs.

A number of reports have appeared of the successful use of "milontin" (N-methyl-*alpha*-phenylsuccinimide; P.M. 334) in the control of petit-mal epilepsy. In order to determine the possible site and mode of action of this drug on the central nervous system the authors have studied its effect at various levels of the cerebrospinal axis and compared it with that of troxidone in a series of experiments on cats carried out at the State Hospital, Traverse City, Michigan.

In doses of 50 to 200 mg. per kg. body weight both milontin and troxidone were ineffective in modifying the patellar reflex in cats. The administration of 100 mg. of milontin per kg. produced marked slowing of the waves and sleep-like spindles in the electroencephalogram (EEG) of cats previously showing the fast activity of a normal waking animal; the same dose of troxidone produced similar but less marked effects. Both milontin and troxidone damped down the fast activity appearing in the EEG following stimulation of the activating centre. No change in the EEG pattern was produced by either drug in cats transected through the mesencephalon (producing the so-called *cerveau isolé*).

The effect of the drugs was then determined on the "after-discharge" resulting from focal stimulation of both the anterior cingulate gyrus and the motor cortex in 4 lightly anaesthetized cats, the stimulus being applied for 5 seconds immediately before the EEG was recorded. The after-discharge was reduced in the anterior cingulate gyrus following the administration of 50 mg. of milontin per kg. body weight and abolished by a dose of 100 mg. per kg.; larger doses were occasionally required for complete abolition of the after-discharge in the motor cortex, but a dose of 100 mg. per kg. almost completely abolished the discharge in the right frontal cortex. In contrast, doses of 400 to 500 mg. of troxidone per kg. were required to abolish the after-discharge in the cingulate gyrus and of 500 to 600 mg. per kg. to abolish that in the motor cortex. The effect of bilateral stimulation was tested on 3 non-anaesthetized cats. The after-discharge was completely abolished by a dose of 100 mg. of milontin per kg., whereas troxidone in a dose of 400 mg. per kg. completely abolished the after-discharge in one cat and almost abolished it in the second of the 2 animals tested.

The authors conclude that in normal dosage neither troxidone nor milontin has a demonstrable effect on the spinal cord. Both drugs have a mild sedative effect and, while apparently equipotent in certain depressant actions unrelated to seizure activity, milontin is more potent in suppressing cortical after-discharge.

Robert Hodgkinson

27. **Pharmacological Properties of Mephentermine, a Sympathomimetic Amine**

D. K. ECKFELD, L. L. ABELL, and J. SEIFTER. *Journal of the American Pharmaceutical Association* [*J. Amer. pharm. Ass.*] **43**, 705–708, Dec., 1954. 13 refs.

Mephentermine [N-methyl-ω-phenyl-tertiary-butylamine] has sympathomimetic properties similar to that of other β-phenyl-ethylamines. It is unique in that it contains no asymmetric carbon atom and therefore does not exist in D- or L- form. It is less toxic for mice than amphetamine or D-desoxyephedrine and more toxic than L-ephedrine. Mephentermine, unlike epinephrine [adrenaline], does not cause hyperglycemia in rabbits.

The pressor response and effect on heart rate due to mephentermine, in intact and vagotomized dogs, are qualitatively and quantitatively similar to those observed after L-ephedrine. Absorption from the frontal sinuses of dogs is minimal and the effect on blood pressure after such instillation is no greater than after L-ephedrine. By constricting the small blood vessels of the nasal mucosa mephentermine is capable of increasing the air space of the nasal passages. Mephentermine has approximately one-third to one-half the potency of amphetamine or D-desoxyephedrine as a cerebral stimulant for chicks, cats, and dogs. It causes no decrease in normal ciliary activity of the trachea, lacks spasmolytic action on smooth muscle of the intestine, causes no anesthesia when applied topically to rabbit eyes, and, in common with other sympathomimetic amines, produces pupillary dilatation. —[From the authors' summary.]

28. **The Action of Phosphorylated Hesperidin on Blood Coagulation**

R. BOURGAIN, C. SYMONS, M. TODD, and I. S. WRIGHT. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **112**, 393–398, Dec., 1954. 4 figs., 9 refs.

Chemotherapy

29. Synergism and Antagonism between Antibiotic Mixtures Containing Erythromycin

A. MANTEN. *Antibiotics and Chemotherapy* [*Antibiot. and Chemother.*] **4**, 1228–1233, Dec., 1954. 2 figs., 25 refs.

Experiments were carried out at the National Institute of Public Health, Utrecht, to determine the effect *in vitro* of combinations of antibiotics containing erythromycin upon 47 strains of coagulase-positive staphylococci. The technique consisted in agar-plate diffusion incorporating paper disks impregnated with various combinations of antibiotics; a second or replica plate was used to assess the degree of bactericidal action in the zones of inhibition on the primary plate.

It was found that the action of erythromycin was antagonistic to penicillin, synergistic with streptomycin, and independent of chloramphenicol and oxytetracycline. *D. Geraint James*

30. Primycin, a New Antibiotic

T. VÁLYI-NAGY, J. ÚRI, and I. SZILÁGYI. *Nature* [*Nature (Lond.)*] **174**, 1105–1106, Dec. 11, 1954.

At the University of Debrecen, Hungary, a new antibiotic has been obtained from a micro-organism isolated from the larvae of the wax moth, *Galeria melonella*. Morphologically, the organism belongs to the genus *Actinomyces*.

Some of the physical and chemical properties of this antibiotic and its active substance ("primycin") are described. Solutions of the purest product obtained so far inhibit the growth of *Staphylococcus aureus* Duncan in concentrations of 0·02 to 0·06 μg. per ml. *In vitro* primycin has a bacteriostatic effect on Gram-positive organisms and mycobacteria and is non-toxic to tissue cultures. The LD for mice is 2·5 mg. per kg. body weight and for rats 10 mg. per kg. The authors state that since the drug appears to be toxic to animals it has been tried only on superficial infections in human subjects; however, good results are claimed.

A. W. H. Foxell

31. Mode of Action of Isoniazid. Part II

W. R. BARCLAY, D. KOCH-WESER, and R. H. EBERT. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 784–792, Nov., 1954. 4 figs., 11 refs.

In some investigations at the University of Chicago the authors have previously demonstrated (*Amer. Rev. Tuberc.*, 1953, **67**, 490; *Abstracts of World Medicine*, 1953, **14**, 453) that tubercle bacilli sensitive to isoniazid become radioactive when incubated with isoniazid containing radioactive carbon (^{14}C). They now show that this does not occur with ^{14}C-labelled nicotinic acid, nicotinamide, or *iso*nicotinic acid, nor if the bacilli have been killed by heat or formaldehyde. The isoniazid binding is increased by the presence of streptomycin or by cold (5° C.), although the rate of uptake is the same at all temperatures for the first 24 hours. Varying the concentration of isoniazid causes changes in uptake, which indicates that the process is one of adsorption—a view consistent with the lack of effect of cooling. The process is contrasted with the binding of penicillin by penicillin-sensitive organisms, which is regarded as a chemical union. *V. J. Woolley*

32. Clinical and Experimental Studies of "Streptoniazid". (Recherches cliniques et biologiques sur la streptoniazide)

—. PIERRE-BOURGEOIS, —. VIC-DUPONT, —. DUBOIS-VERLIÈRE, and G. DELMAS. *Revue de la tuberculose* [*Rev. Tuberc. (Paris)*] **18**, 891–897, 1954.

"Streptoniazid", described as the *iso*nicotyl hydrazone of streptomycin, is a compound of isoniazid and streptomycin. In this paper the authors report the results of a clinical and laboratory trial of this recently introduced substance which appear to be similar to those obtained by the simultaneous use of its two components. While it was tolerated well enough locally, some systemic reactions occurred, these being minor in 34 (43%) of the 80 patients treated, but sufficiently severe to warrant stopping treatment in 13 cases. In addition to the well-known toxic effects of streptomycin and isoniazid, such as digestive and labyrinthine disorders, a persistent optic neuritis developed in one case and transient cerebral oedema in another during treatment with the new compound.

Intramuscular injection was the most satisfactory method of administration, slow intravenous infusions (sometimes containing also PAS) causing a greater number of minor side-effects. Intravenous injection was not well tolerated and should be avoided. The therapeutic results after treatment for up to 3 months with 1·23 g. of the compound either daily or once every 2 or 3 days during the first, second, and third months were similar to those obtained with streptomycin or isoniazid, either alone or together, and were slightly inferior to those obtained with infusions of isoniazid and PAS. Laboratory studies *in vitro* and *in vivo* (in guinea-pigs) also showed that the activity of the compound differed little from that of its constituent substances.

[This was not a fully controlled clinical trial, but the results seem to indicate that this compound has no special virtues and may even have disadvantages from the point of view of toxicity.] *Derek R. Wood*

33. S-Ethyl-L-cysteine, a Member of a New Group of Antituberculous Compounds

M. SOLOTOROVSKY, S. WINSTEN, E. IRONSON, H. D. BROWN, and H. J. BECKER. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 806–811, Nov., 1954. 18 refs.

Infectious Diseases

34. **On the Aetiology and Delineation of Sarcoid.** (Zur Ätiologie des Morbus Boeck und zur Abegrenzung seines Formenkreises)

K. W. KALKOFF. *Zeitschrift für Haut- und Geschlechtskrankheiten* [*Z. Haut- u. GeschlKr.*] **18**, 1–9, Jan. 1, 1955.

Writing from the University Dermatological Clinic, Marburg, the author points out that it is important to differentiate clearly between a sarcoid reaction, which may be due to a variety of stimuli, and true Boeck's sarcoid. The latter is characterized above all by being a systemic disease. As yet there is no certainty as to the cause of Boeck's sarcoid, but in the author's opinion the finding of the tubercle bacillus may be of aetiological significance. Sarcoid reactions occurring in leprosy and syphilis are always localized, but those due, for example, to exposure to beryllium show some signs of generalization and thus approximate to the true Boeck's sarcoid in some respects. The possibility of isolated hilar adenopathy, with or without erythema nodosum, being an early and often transient form of sarcoid disease is discussed. The author has found that the hilar nodes are often more prominent on the right side, owing to the normally greater amount of lymphatic tissue on that side. Sometimes the right supraclavicular nodes are palpable in these cases, and this finding is of diagnostic help in the presence of skin lesions. It is stressed that hilar adenopathy is sometimes present when the disease does not in other respects involve the respiratory system.

Of other conditions which may be confused with Boeck's sarcoid the author mentions two: the subcutaneous multiple nodules of Darier–Roussy, and cheilitis granulomatosa. The former occurs in tuberculin-positive individuals and shows some tendency to necrosis; it is therefore regarded as an intermediate form between sarcoid and erythema induratum. The latter condition shows histological similarities to sarcoid, but so far no signs of systemic disease have been reported, and it is thought prudent to await such evidence before including it amongst the clinical varieties of sarcoidosis. *G. W. Csonka*

35. **The Effect of Vitamin B_{12} and Folic Acid in the Treatment of Viral Hepatitis**

R. E. CAMPBELL and F. W. PRUITT. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 8–15, Jan., 1955. 3 figs., 19 refs.

The authors describe a controlled study of the effect of administration of vitamin B_{12} (cyanocobalamin) and folic acid to patients suffering from viral hepatitis which was carried out at the U.S. Army Hepatitis Center in Japan during 1950 and 1951. The trial was based on the theory [only partly backed by experimental evidence] that folic acid and vitamin B_{12} are directly or indirectly necessary at certain stages of the synthesis of nucleic acid, one of the first signs of liver damage in rats given carbon tetrachloride being the disappearance of nucleic acid compounds from the centre of the lobules.

In a previous paper (*Amer. J. med. Sci.*, 1952, **224**, 252; *Abstracts of World Medicine*, 1953, **13**, 105) the authors presented evidence suggesting that the administration of vitamin B_{12} will shorten the course of viral hepatitis in man. In the present trial 88 men, all suffering from viral hepatitis, were divided into two equal groups, comparable as regards colour, age, clinical picture, and biochemical findings. Both groups were given a diet containing 150 g. of protein, 350 g. of carbohydrate, and 100 g. of fat reinforced with milk to give a total daily intake of 4,000 Calories, and one group received, in addition, 30 μg. of vitamin B_{12} intramuscularly on alternate days and 5 mg. of folic acid 3 times daily by mouth for the first 10 days. At weekly intervals the patients' symptoms and signs were recorded, the total serum bilirubin content estimated, and liver function tests performed. On the basis of these findings the average duration of the illness in the experimental group was 47·5 days and in the control group 57·2 days. The difference was more marked amongst patients whose total serum bilirubin level was above 5 mg. per 100 ml., and especially when it was above 15 mg. per 100 ml., when it amounted to 17·2 days.

The authors discuss the findings of other investigators which suggest a link between vitamin B_{12} and folic acid and the choline-oxidase and coenzyme-A systems, which are essential for satisfactory liver function, and from which they conclude that "there are ample theoretical reasons why vitamin B_{12} and folic acid should be of benefit in hepatic repair". *P. I. Reed*

36. **The Specific Treatment of Whooping-cough and Changes in Mortality from the Disease in Hospital.** (Le traitement curatif de la coqueluche et l'évolution de la mortalité coquelucheuse en milieu hospitalier)

J. MARIE, H. BOISSIÈRE, G. SÉE, E. ELIACHAR, P. GURAN, and S. MASSELIN. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **30**, 3589–3594, Oct. 22, 1954.

The over-all mortality from whooping-cough among patients treated at the Hôpital des Enfants-Malades, Paris, during the period 1941–6, when there was no specific treatment, was 10·38% for 1,052 cases; during the period 1950–2, when specific treatment was available, it was 3·8% for 206 cases. The decline in mortality in different age groups was as follows: 0 to 6 months, from 33·8 to 8·6%; 6 months to 1 year, 23 to 4·5%; 1 to 2 years, 16 to 4·1%; 2 to 5 years, 4·7 to 1·1%; and over 5 years, 2·05% to *nil*.

This striking diminution in mortality could not be accounted for by an improvement in the general health of the child population, by a diminution in virulence of the disease, or by better hospital conditions. The

authors therefore suggest that it must be the result of modern specific treatment, namely immunization and the use of antibiotics, particularly streptomycin, chloramphenicol, aureomycin, and oxytetracycline, given either singly or in association. Their various methods of treatment are given in some detail. They note that among 30 patients treated with chloramphenicol orally in daily doses of 50 mg. per kg. body weight for 2 to 3 weeks, only one case of transient granulocytopenia was observed. Aureomycin or oxytetracycline was given, orally, only in 8 cases in which there was some fear of agranulocytosis developing. The authors recommend strongly what they term the " triple treatment ", consisting in the administration of hyperimmune serum, chloramphenicol by mouth, and streptomycin intramuscularly, for all severe or complicated cases of whooping-cough.

The results of treatment are analysed, with particular reference to the 31 severe or complicated cases in the series. Thus of 7 infants with severe apnoeic attacks, all recovered in less than 15 days; among 13 patients with bronchopneumonia there was one death from anoxic convulsions; of 6 patients with " encephalitis " (convulsions and status epilepticus), 5 died, confirming the lack of response to all treatment in such cases; and of 5 cases with such miscellaneous conditions as toxaemia, dehydration, cor pulmonale, or tuberculous bronchopneumonia, all were fatal. The incidence of complicated cases fell notably in the second period, being 35% in the period 1941–6, and only 10% in the period 1950–2. The results obtained with various antibiotics, alone or in combination, in the uncomplicated cases showed very little difference.

L. J. M. Laurent

37. Sonne Dysentery Treated with Tetracycline. A Comparison with Phthalyl Sulphathiazole and Oral Streptomycin

J. D. Abbott and H. E. Parry. *Lancet* [*Lancet*] **1**, 16–18, Jan. 1, 1955. 9 refs.

Of 84 bacteriologically proved cases of Sonne dysentery admitted to Monsall Hospital, Manchester, between June, 1953, and August, 1954, 27 were treated with tetracycline, 32 with phthalylsulphathiazole, and 25 with streptomycin, all given by mouth. The dose of tetracycline for patients under the age of 5 was 125 mg., from 5 to 15 years 250 mg., and over 15 years 500 mg., given 6-hourly for 7 days in each case. Phthalylsulphathiazole was given 6-hourly for 7 days in a dose of 0·5 g. to those under 5 years, 1 g. to those aged 5 to 15 years, and 2 g. to those over 15 years. Streptomycin was given in doses of 0·5 g. twice a day for 3 to 8 days regardless of age.

Treatment was successful in only one-third of the patients given phthalylsulphathiazole or streptomycin, whereas there was only one failure with tetracycline.

[This study was not adequately controlled, since the three drugs were not given simultaneously, streptomycin being used over the whole period and the other two only during the last 5 months. Diseases vary in severity from time to time, partly because of changes in the virulence of organisms, and it is unwise to attempt to compare the results of treatment with one drug at one time with those of treatment with another drug at another time. The use of the alternate-case method or, better still, random sampling would have given more valid grounds for comparison.] *R. S. Illingworth*

38. Observations on the Natural Reservoir of *Leptospira icterohaemorrhagiae*. (Наблюдения над основным резервуаром иктеро-геморрагических лептоспир)

N. I. Amosenkova and E. M. Popova. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Z. Mikrobiol.*] 67–70, No. 12, Dec., 1954. 10 refs.

A search for grey rats (*Rattus norvegicus*) carrying *Leptospira icterohaemorrhagiae* was carried out in a community which had suffered from an outbreak of Weil's disease lasting for several years, although the incidence of new cases was now on the decline. During the period June, 1946, to December, 1947, 1,172 rats were caught in large food stores. Emulsions made from the kidneys were cultured and examined microscopically with dark-ground illumination, while serum from the animals was used for the standard agglutination and lysis reactions.

In this way 25% of all rats caught were shown to be infected, approximately the same proportion of infected rats being found during each quarter of the year. Thus the seasonal incidence of the infection in man does not appear to be due to a similar seasonal incidence in rats. Moreover, in spite of this constant carrier rate among the natural hosts the incidence of the infection in the human population continued to decrease. Of the diagnostic methods used, the serological tests gave the highest number of positive results, closely followed by culture, while the number of positive diagnoses made by direct microscopy was less than half that made by either of the other methods. *K. Zinnemann*

39. The Carrier Rate of *Leptospira canicola* in Wild Rats on the Island of Sakhalin. (Носительство лептоспир типа canicola среди диких крыс на о. Сахалине)

I. S. Bezdenezhnykh and D. L. Shafershtein. *Журнал Микробиологии, Эпидемиологии и Иммунобиологии* [*Z. Mikrobiol.*] 71–72, No. 12, Dec., 1954. 10 refs.

The serum of 14 out of 228 grey rats (*Rattus norvegicus*) caught on Sakhalin Island gave positive agglutination and lysis reactions with 3 different laboratory strains of *Leptospira canicola*. One strain of *L. canicola* was isolated from an emulsion of kidney prepared from a batch of rats.

This is the first demonstration in the Soviet Union that the grey rat is a carrier of *L. canicola*. The authors conclude that eradication of this rat must be one of the main measures in the prevention of canine leptospirosis and its transmission to man. *K. Zinnemann*

40. Infection with *Cryptococcus neoformans* in Man. Report of Two Cases

A. Beck, M. W. Hutchings, A. R. Makey, and I. M. Tuck. *Lancet* [*Lancet*] **1**, 535–538, March 12, 1955. 7 figs., 11 refs.

Tuberculosis

DIAGNOSIS AND PROPHYLAXIS

41. A Comparison of Vaccination with Vole Bacillus and B.C.G. Vaccines

H. W. O. Frew, J. R. Davidson, and J. T. W. Reid. *British Medical Journal* [*Brit. med. J.*] **1**, 133–136, Jan. 15, 1955. 2 refs.

In this report from the Orphan Homes of Scotland, Bridge of Weir, Renfrewshire, the authors compare the ease of administration, Mantoux conversion rates, and complications of vaccination with B.C.G. and vole bacillus (V.B.) vaccine. One group of 288 children, selected at random, were given B.C.G., and another group of 280 received V.B. vaccine, the latter as reconstituted dried vaccine in 1951, as a liquid vaccine in 1952, and as half-strength liquid vaccine in 1953. In 1951 those under 5 years of age were given V.B. vaccine by the intradermal method, but on all other occasions this vaccine was given by multiple puncture; in all cases B.C.G. was given intradermally.

Mantoux conversion generally occurred more quickly with B.C.G. vaccine, but by the end of 6 weeks almost 100% of both groups had converted. Intradermal V.B. vaccination produced more severe local reactions than did intradermal B.C.G., but when V.B. was given by multiple puncture the immediate local reaction was slight. At 6 months and 1 year there was little difference between the two groups in regard to percentage of reversions, but at the end of 2 years Mantoux reversions to negative were higher in the B.C.G. group, and in this group the number of those reacting only to a large dose (100 units) of old tuberculin was also greater at this time. Examination of the vaccination area at 1 and 2 years revealed indurated areas of a lupoid character in some cases in which V.B. vaccine had been given by multiple puncture, whereas this complication was not observed in those given B.C.G. Although vaccination with V.B. vaccine has certain advantages, the authors "regard the rate of these reactions to be too high to permit of the routine use of the vaccine until these difficulties have been overcome". *T. M. Pollock*

42. Quantitative Aspects of the Intradermal Tuberculin Test in Humans. II. The Relative Importance of Accurate Injection Technique. [In English]

J. Guld. *Acta tuberculosa Scandinavica* [*Acta tuberc. scand.*] **30**, 16–36, 1954. 2 figs., 8 refs.

In this further study from the World Health Organization Tuberculosis Research Office, Copenhagen, of some of the fundamental problems connected with tuberculin surveys and B.C.G. vaccination, the following factors concerned with the injection of tuberculin in performing the Mantoux test were investigated in order to determine how far they influence the resulting tuberculin reaction: (1) test site, (2) volume and depth of injection, (3) the dose of tuberculin, and (4) the concentration of the solution used.

It was found that the size of the reaction was the same at all four commonly used sites on the forearm, and was little affected by the depth at which the injection was given, although after deeper injections the results were less easy to read. For strictly intradermal injections of tuberculin considerable pressure is required, and it is common to find some leakage between the plunger and barrel of the tuberculin syringe: hence the estimation from the scale marked on the syringe of the volume of tuberculin injected is liable to error, sometimes gross. In practice, therefore, it is usual to estimate the amount of fluid injected by the size of the resulting weal. Workers continuously engaged in tuberculin testing claim that they can estimate accurately the diameter of the intradermal weal produced by injection of a volume of 0·1 ml., but the accuracy of this estimation is shown to be subject to appreciable variation between operators.

It is therefore concluded that to increase the accuracy of tuberculin testing the provision of leak-proof syringes is essential. Some indirect evidence was also obtained to suggest that, whereas the stronger reactions to tuberculin depend only on the weight of P.P.D. tuberculin injected, the weaker reactions seemed to depend on the concentration of the solution, indicating that the differentiation between positive and negative reactions may not be greatly affected by variations in the volume injected. *J. E. M. Whitehead*

43. A Tuberculosis Survey in Broadmoor: Experience with the Heaf Multiple-puncture Tuberculin Test

B. C. Thompson. *Tubercle* [*Tubercle* (*Lond.*)] **36**, 18–20, Jan., 1955. 1 ref.

A survey of the staff and patients of the Broadmoor Institution for the criminally psychotic was carried out by mass miniature radiography and by the multiple-puncture tuberculin test of Heaf, which corresponds to a Mantoux test with at least 10 tuberculin units. Of the 742 patients (including 84 women) who were radiographed, lesions suggestive of pulmonary tuberculosis were found in 41 (all male), but only in one case was an active process with positive sputum shown to be present; of the remainder, 12 had healed or obsolete lesions and 21 remained under observation for inactive lesions. Among the 266 members of the staff (including 39 women) one case of pulmonary tuberculosis, probably active but with negative sputum, was found. The tuberculin test was performed on 717 patients (including 83 women), of whom 38 (5 women and 33 men) gave a negative reaction. Negativity of the reaction was not related to age or to duration of confinement in the institution. However, it is suggested that the relatively low incidence

of active disease in this isolated community " may be attributed in part to the support of natural resistance by good living conditions ". *Franz Heimann*

44. Observations on the Heaf Multiple-puncture Test
K. N. IRVINE. *Tubercle* [*Tubercle (Lond.)*] **36**, 21–22, Jan., 1955. 2 refs.

From a comparison of the results of the Mantoux test and the multiple-puncture tuberculin test of Heaf in 869 persons of all ages the author comes to the conclusion that the latter is a reliable " one-shot " test. When the results were read after 3 to 4 days the Heaf test gave a positive reaction in 99 to 100% of cases reacting to the Mantoux test with 1 or 10 units, but in only 82% of those reacting to 100 units, indicating a lesser degree of sensitivity. When the results were read after 7 days the Heaf test was on the whole disappointing in comparison with the Mantoux test.

Franz Heimann

RESPIRATORY TUBERCULOSIS

45. Observations on the Treatment of Pulmonary Tuberculosis at the Present Time
J. L. LIVINGSTONE. *British Medical Journal* [*Brit. med. J.*] **1**, 243–250, Jan. 29, 1955. 10 figs., 18 refs.

In this paper from King's College and Brompton Hospitals, London, the author reviews the treatment of pulmonary tuberculosis in the light of recent advances and compares his own results with those of other clinicians. He considers that artificial pneumothorax still has a place in the treatment of suitable cases, but that it should be restricted to those in which the cavity is less than 4 cm. in diameter and there is no evidence of endobronchial disease; it should also be avoided if there is any likelihood of mediastinal displacement after the lung is healed. He emphasizes that since empyema is a frequent complication there should be no hesitation in abandoning an unsuitable artificial pneumothorax.

Pneumoperitoneum with phrenic crush, particularly if preceded by chemotherapy and postural retention, is considered to be of value, especially in advanced cases. Of 68 of the author's cases in which pneumoperitoneum with phrenic crush was carried out, in most of which chemotherapy was not employed, the results were classified as " good " in 32, " failed " in 20, and " not proven " in 14. As he points out, the results would have been better had chemotherapy been given. Discussing lucite plombage, he states that the results of this technique have so far been good in 20 out of 27 cases, but that it is too early " to be sure that the foreign body in the chest wall will not give trouble ", although he thinks this unlikely. Resection carries a low mortality, but here again the follow-up period in the author's cases has not been long enough for an adequate assessment to be made.

Rest in bed is still of first importance in treatment, especially for patients awaiting admission to hospital; it is during this waiting period that the disease often extends. Ideally, each patient should be under the care of the same physician throughout treatment, especially when refills are necessary.

[This is a balanced and comprehensive survey, containing an abundance of interesting statistical matter.]

Paul B. Woolley

46. Current Therapy in Pulmonary Tuberculosis in the United States
H. G. TRIMBLE. *British Medical Journal* [*Brit. med. J.*] **1**, 250–253, Jan. 29, 1955. 10 figs.

In this paper from Stanford University, California, the author describes an investigation carried out under the auspices of the American College of Chest Physicians. The case history and one radiograph of 10 tuberculous patients whose sputum was positive for tubercle bacilli were sent to 100 distinguished American chest physicians together with a questionary inquiring how each would treat these cases. From the replies received the author draws some conclusions regarding recent tendencies in the treatment of tuberculosis in the United States.

It was found that almost 100% of the physicians recommended the use of antibiotics whatever the nature of the pulmonary lesion, but there was no general agreement as to how long these drugs were to be administered. The drugs of choice were limited to streptomycin, PAS, and isoniazid, of which most preferred the first two in combination. Only a few physicians (2%) favoured the induction of artificial pneumothorax, collapse by pneumoperitoneum being preferred by 20%. [As in Great Britain, the use of artificial pneumothorax seems to be dying out.] It was clear that the physicians consulted showed a leaning towards the more frequent use of surgical intervention, and a far greater percentage preferred resection to thoracoplasty in treatment of the average case. The actual treatment given by the author himself in these cases was complete bed rest and chemotherapy, with or without collapse therapy, for about 18 months; if bronchoscopy revealed little or no improvement surgical procedures were then considered. He warns against the use of artificial pneumothorax in the presence of endobronchial disease, and prefers pneumoperitoneum as a medical collapse procedure.

[Details of the treatment recommended by the consulted physicians are presented in respect of only 5 of the cases, and although a comparison is made with a similar inquiry made in 1948 on the same 10 cases, no bibliographical reference to this inquiry is given.]

Paul B. Woolley

47. Pulmonary Primary Tuberculosis in Childhood
C. H. M. WALKER. *Lancet* [*Lancet*] **1**, 218–224, Jan. 29, 1955. 1 fig., 31 refs.

The belief that the future prospects of children with healed primary tuberculosis are universally good has been questioned. The author therefore carried out a long-term follow-up study of over 750 children with an active primary lung complex seen in the out-patient departments and wards of the Hospital for Sick Children, Great Ormond Street, and of University College Hospital, London. For various reasons only 538 of the cases were included in this report. Some 50% of the patients

were followed up for 2 years or more, 20% for one to 2 years, and 30% were observed for less than one year, this proportion including, of course, most of the 55 patients who died early.

No complications were observed in 30% of the patients, radiological changes suggestive of consolidation or segmental collapse were found in 48%, and serious complications such as miliary tuberculosis or meningitis developed in 19%, most of these patients being under 6 years of age. Bronchiectasis was diagnosed in 2% of the patients, but as bronchography was not performed in all cases the author believes this figure may be inaccurate. Tubercle bacilli were found in the gastric washings in only 16% of the cases. There was a history of contact with a known case of active pulmonary tuberculosis in 54%.

Treatment consisted of rest in bed in hospital followed by a period at a convalescent home, but a few children were treated as out-patients throughout when circumstances permitted. Specific chemotherapy was given to only 19% of 477 of the patients who survived, including all cases of meningitis and miliary tuberculosis and most of those with local dissemination. Bronchoscopy was undertaken in 44 cases, but the value of this procedure was limited and in only 11 cases was it beneficial. Lobectomy was performed in 7 instances; although this operation is well tolerated by children it should, in the author's view, be reserved for patients who have not responded to conservative treatment. As stated above, there were 55 deaths, 26 of these occurring during the first 3 months of observation and a further 18 within one year. Only one of the children who had been observed for over 2 years died. The author concludes that a mortality of 10%, even in this selected series of more serious hospital cases, is in agreement with previous conclusions drawn from similar studies that the prognosis of pulmonary primary complex in childhood is relatively good. *R. M. Todd*

48. Tuberculous Cavitation of the Apical Segment of the Lower Lobe

H. J. H. Hiddlestone and A. J. Taylor. *Thorax* [*Thorax*] **9**, 344–349, Dec., 1954. 16 refs.

In an endeavour to discover prognostic criteria and therapeutic indications the authors have reviewed 143 cases of cavitation of the apical segment of the lower lobe treated at the Brompton Hospital, London, between 1935 and 1950. In all of them the site of the disease had been accurately located by lateral radiographs or tomography. The records were analysed in respect of age, sex, sputum state, extent of disease, erythrocyte sedimentation rate, and response to therapy. The patients were of all ages from 11 to 55, but 66 were between 21 and 30, and more than two-thirds (103) were female. Treatment had varied from simple bed rest to the induction of artificial pneumothorax, phrenic crush, and a variety of surgical procedures including thoracoplasty and lobectomy; only a small proportion of the patients had received antibiotics. All cases were followed up for a minimum of 4 years, and some of the earliest for as long as 18 years.

The disease was found to be more common in the right lung (95 out of the 143 cases). No pathognomonic symptom was discovered, but 25% of the patients had complained of a low, posterior, dull or pleuritic pain on the affected side, and it is suggested that this may be a guide to location. The effect of different methods of treatment is given in detail in a series of tables; on the whole, artificial pneumothorax appeared to have given the best results, even without preliminary antibacterial treatment. In combination with the latter, however, resection also proved satisfactory; in 10 cases this procedure was carried out after failure of the primary treatment.

The authors discuss the difficulties of diagnosis and also make reference to the theory that the apex of the lower lobe of the lung is the least well ventilated, being poorly served by both diaphragmatic and costal respiratory movement. It is suggested that the less effective movement of the diaphragm in females may account for the greater frequency of this type of disease in women. *R. J. Matthews*

49. The Healing of Tuberculous Lesions in the Lung with Persistence of Cavitation. (La guérison des cavernes tuberculeuses du poumon avec persistance de la cavité) A. Bernou, R. Goyer, L. Marécaux, J. Tricoire, and J. Butez. *Poumon* [*Poumon*] **10**, 573–592, Nov. 13, 1954. 4 figs., 15 refs.

The authors discuss the apparent "cure" of tuberculosis in cases which still show radiological evidence of cavitation. They consider that some cavities may be "sterilized" and no longer contain any active lesion, while in others the draining bronchus becomes blocked so that the cavity is excluded from the bronchial tree; the former type of cavity has a supple, thin wall which may be covered by granulation tissue. However, in some cases cleansing of the cavity is not complete and small caseous areas may remain in the cavity wall, especially in the area of the draining bronchus, or there may be caseation in a diverticulum of the cavity; that this occurs has been shown by examination of resected specimens. In the authors' opinion such cavities have appeared more frequently since the advent of chemotherapy, and especially of isoniazid, and reports of 5 cases are presented in which, after such treatment, the sputum was persistently negative but a thin-walled cavity remained. This cavity usually only became bullous in character after a sudden distension which seemed to coincide with the sputum becoming negative; later the cavity returned to its original size. A further case in which the cavity persisted is cited, but here it had irregular thickening of the walls, and the authors believe that this occurs in old-standing cases where there has been much fibrosis.

In general these cavities resemble emphysematous bullae except that the walls are usually thicker. It may be difficult to differentiate them from cavities whose draining bronchus is blocked, but this can sometimes be done by the intracavitary injection of contrast medium or methylene blue. In most cases, however, the cavity can be diagnosed with certainty only by examination of

serial radiographs. In discussing the prognosis and treatment in such cases the authors report that several patients have remained well for periods up to 10 years. They conclude that a favourable prognosis depends on the total sterilization of the wall of the cavity, and point out that cavities with irregular walls often contain a residual tuberculous lesion. When the draining bronchus of the cavity is closed the prognosis is poorer, but in all such cases the state of the other parts of the lung must be considered. If the cavity is smooth the treatment advised is merely careful surveillance, but if the cavity walls are irregular a stricter watch is necessary and the induction of artificial pneumothorax may be required. If the cavity is very large surgical resection is perhaps the best treatment. *G. M. Little*

50. Chemotherapy and Cavity Wall. Histological Observations

W. PAGEL and F. A. H. SIMMONDS. *Tubercle* [*Tubercle (Lond.)*] **36**, 2–15, Jan., 1955. 12 figs., 17 refs.

The authors review 3 cases of pulmonary tuberculosis in which certain new features of cavity healing as the result of prolonged chemotherapy were observed in post-mortem or operation specimens of lung. Cavities usually heal by closure of the draining bronchus and inspissation and calcification of the contents, by scar formation, or by fibrous healing of the tuberculous wall with epithelization from the patent draining bronchus. The distinguishing features of the cases described were the replacement of the tuberculous and caseous cavity wall by ordinary granulation tissue, the formation of a fibrotic lining without epithelization, and the occurrence of foreign-body granulomata in the form of small " warty " elevations on the fibrotic lining. The authors assume that these findings are the result of a direct action of chemotherapy on the tuberculous wall of the cavity. *Franz Heimann*

51. Immunotherapy, Chemotherapy, and Antibiotic Therapy in the Treatment of Chronic Pulmonary Tuberculosis. (Associazione immuno-chemio-antibiotica nella terapia della tubercolosi polmonare cronica)

G. FEZIG, M. LUCCHESI, and G. SPINA. *Rivista della tubercolosi e delle malattie dell'apparato respiratorio* [*Riv. Tuberc.*] **2**, 519–547, Nov.–Dec., 1954. 41 figs., 22 refs.

At the Forlanini Institute, Rome, 35 patients suffering from chronic pulmonary tuberculosis with cavitation, who had been treated with streptomycin in combination with isoniazid without success, were given intravenous injections of Petragnani's preparation " fenbettacin " in gradually increasing doses twice weekly. This preparation is derived from a phenolic extract of tubercle bacilli by treatment with acetone.

The authors distinguished four types of reaction after its administration. (1) An immediate reaction, noted in 9 cases 2 to 6 hours after the injection, was characterized by rigor, vomiting, and headache, the temperature rising to between 38·5° and 40° C. (101·4° to 104° F.) and returning to the previous level after 12 hours. (2) A second type of reaction, observed in 11 patients, resembled a tuberculin reaction; the symptoms started 10 hours after the injection and lasted for 48 to 72 hours, the patients complaining of headache and pain in the joints. (3) The third type was a combination of the two former and was seen in 3 patients. (4) A reaction consisting of slight headache, lassitude, and pain in the joints, with only slight rise of temperature, was observed in 12 cases. The results of this vaccine therapy were satisfactory, in that 13 patients recovered, 14 improved, 4 remained stationary, and only 4 showed deterioration. The treatment is recommended for infiltrative lesions, for cases of chronic miliary tuberculosis with and without cavities, extrapleural pneumothorax, and residual cavities after thoracoplasty. The importance of careful selection of cases is stressed.

Franz Heimann

52. Testosterone in Chronic Tuberculosis

R. L. GRIFFITH and R. H. LINN. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **70**, 1020–1029, Dec., 1954. 32 refs.

The authors have investigated the value of testosterone propionate as an anabolic agent in the treatment of the cachexia of chronic pulmonary tuberculosis. At the U.S. Public Health Service Hospital, Seattle, Washington, 17 male patients who were unable to gain weight were given the drug intramuscularly, some receiving 25 mg. and others 50 mg. 3 times a week for periods varying from 1½ to 13 months. All the patients were also receiving antituberculous drugs. Their ages ranged from 29 to 60, but no correlation was apparent between the age of the patient and the results.

While the gains in weight were not statistically conclusive, the authors judged that the response in 7 cases was good, in 3 fair, in 5 doubtful, and in 2 poor. The highest gain was 30 lb. (13·6 kg.), and the gains were greater among those receiving the 50-mg. doses, the average gain in this group being 13·3 lb. (6 kg.) compared with a mean of 7·7 lb. (3·4 kg.) in the group given 25 mg. The testosterone was well tolerated; there were no local or general complications and no endocrine upset. No spread of the tuberculous process occurred during treatment or as a result of it, but 5 patients lost weight when the injections were discontinued.

[Although these patients did not know what they were being given, it is at least possible that the effect of suggestion or the natural processes of recovery rather than testosterone was the factor responsible for the gains reported.] *I. M. Librach*

53. The Use of Oxytetracycline in Preventing or Delaying Isoniazid Resistance in Pulmonary Tuberculosis

S. M. STEWART, F. W. A. TURNBULL, and J. W. CROFTON. *British Medical Journal* [*Brit. med. J.*] **2**, 1508–1511, Dec. 25, 1954. 22 refs.

The authors, from the University of Edinburgh, report their experience with oxytetracycline and isoniazid in the treatment for upwards of 3 months of 33 patients with chronic pulmonary tuberculosis (most of them with cavitation). All the patients received isoniazid in a dosage of 100 mg. twice daily; in addition 10 received 1 g. daily of oxytetracycline, 13 received 2 g. daily, and

10 received 5 g. daily. A group of 17 similar patients who had been treated with isoniazid only served for comparison.

Sputum conversion occurred in about half of those receiving both drugs and in one-third of those given isoniazid only. Isoniazid-resistant bacilli were isolated from the sputum of 5 of the 10 patients given 1 g. oxytetracycline, 6 of the 13 given 2 g., and 12 of the 17 given isoniazid alone. Of the 10 patients treated with 5 g. of oxytetracycline, 3 developed resistance 5 months after the start of treatment. There was no difference between the three groups in clinical and radiological progress. One patient developed intractable diarrhoea and vomiting, but otherwise there were no serious ill effects. Oxytetracycline resistance was not encountered.

The authors conclude that although a dosage of 5 g. daily of oxytetracycline may delay or even prevent the development of isoniazid resistance, this drug with isoniazid is probably less effective than a combination of streptomycin or PAS with isoniazid. Oxytetracycline is also very expensive.

[The investigation appears to have been thorough and the report is clear and concise, with a very fair discussion and conclusion.] *R. J. Matthews*

54. **The Results of Treatment of Pulmonary Tuberculosis with Isoniazid and PAS in Combination for Three Months.** (Résultats du traitement de la tuberculose pulmonaire par isoniazide et P.A.S. appliqués en association pendant trois mois)

E. BERNARD, B. KREIS, A. LOTTE, E. LEJOUBIOUX, and J. L. JULLIEN. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **18**, 841–850, 1954. 4 figs., 5 refs.

Previous papers from the same source (Lotte and Poussier, *Rev. Tuberc.* (*Paris*), 1953, **17**, 1, and Bernard *et al.*, *Rev. Tuberc.* (*Paris*), 1954, **18**, 149; *Abstracts of World Medicine*, 1953, **14**, 197, and 1955, **17**, 102) have reported the results of treatment of pulmonary tuberculosis with isoniazid in 199 cases and with isoniazid, streptomycin, and PAS in combination in 121 cases. These results are now compared with those obtained with isoniazid and PAS in combination in a further series of 103 cases treated at the Hôpital Laennec, Paris. A 3-month course of drug therapy was given, the dose of isoniazid being 5 mg. per kg. body weight daily and that of PAS 15 g. daily, either by the intravenous or the oral route. The three series were comparable as regards the age distribution of the patients and the type of disease treated. After 3 months' treatment 13·5% of the patients in this third series were sputum-negative compared with 74% before chemotherapy, considerable radiological improvement had occurred in 32% of the cases, and a definite change in cavity size in 35·5%.

It was found that the three treatment regimens gave comparable results in respect of radiological appearances and sputum-conversion rates. However, with combined therapy the incidence of drug-resistance was less than with isoniazid alone, there being no significant difference in this respect between the double and the triple combination, both methods delaying the emergence of resistant bacteria equally well. *Thomas Marmion*

55. **Results Obtained with Prolonged Chemotherapy (Six Months to Two Years) in Common Types of Pulmonary Tuberculosis.** (Résultats obtenus par les traitements antibiotiques prolongés (six mois à deux ans) dans la tuberculose pulmonaire commune)

G. BROUET and J. MARCHE. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **18**, 851–890, 1954. 4 figs., bibliography.

While pulmonary tuberculosis can often be cured rapidly if the disease is treated in its early stages, many cases of late and chronic disease, and even some recent cases, require long-term chemotherapy. Between 1951 and 1954 the authors have treated 200 cases, 150 of recent and 50 of chronic tuberculosis, with courses of chemotherapy lasting from 6 months to 2 years without interruption. Streptomycin, PAS, and isoniazid were given together to 132 patients, streptomycin and PAS to 15, and isoniazid alone to 53. The best results were obtained in the series treated with isoniazid, and the authors consider that this drug is the foremost of all antituberculous agents in respect of rapidity of bacterial regression and of cavity closure. Treatment with the triple combination also gave good results over all periods and is considered superior to treatment with streptomycin and PAS. The proportion of cases in each group in which the result was classed as "very good" or "good" at the end of various intervals is given as follows.

Period of Treatment (months)	Streptomycin + Isoniazid + PAS		Isoniazid only		Streptomycin + PAS	
	No. of Cases	% "Good" Results	No. of Cases	% "Good" Results	No. of Cases	% "Good" Results
6	132	39·9	53	50·8	15	19·9
9	103	54·5	33	60·5	5	40·0
12	80	72·5	21	76·2	1	—
15	57	73·0	9	77·7	1	—
18–24 ..	29	72·3	6	83·2	—	—

Cavity closure was obtained in two-thirds of the early cases and in just over one-third of the chronic cases, while nearly one-half of the latter showed radiological and bacteriological improvement. In recent cases cavity closure occurs twice as frequently between the sixth and twelfth months of treatment as at any other time, and it is during this period that the decision must be made whether to employ ancillary methods to promote closure or to perform excision. The most important prognostic index in tuberculosis is the length of time the disease has been present. In the present series long-term chemotherapy and conservative methods gave a fully satisfactory result in one-half of the early cases treated, one-quarter require a further period of observation before a final decision can be reached, and the remaining one-quarter require major or minor surgery.

[This is an important article and should be read in its entirety; it includes discussions of the general principles of collapse measures, the significance and prevention of side-reactions, and some of the social problems that arise during the treatment of the chronic tuberculous patient. A very complete bibliography is appended.] *Thomas Marmion*

56. **The Treatment of Tuberculous Serofibrinous Effusions with ACTH.** (Le traitement des épanchements séro-fibrineux tuberculeux par l'A.C.T.H.)
E. LEBACQ and A. TIRZMALIS. *Revue de la tuberculose* [*Rev. Tuberc.* (*Paris*)] **5**, 898–908, 1954. 20 refs.

The authors report the results of treatment with ACTH (corticotrophin) in various forms of serofibrinous tuberculosis. When given intravenously the dose employed was 10 mg. a day, a Thorn test being carried out beforehand. By intramuscular injection the authors gave 80 mg. a day, divided into 4 injections, for 3 days and then reduced the dose gradually to 40 mg. a day. The period of treatment never exceeded 24 days, the average being about 17 days; in very favourable cases response to ACTH was obtained in 3 days. Transitory hypertension was the only toxic sign noted.

Remarkable success was obtained in 6 out of 9 cases of acute pleural effusion, with a rapid reduction of temperature and loss of fluid within 3 weeks. The 4 cases of chronic pleural effusion treated did not respond to the drug. ACTH was also given in 3 cases of tuberculous pericarditis in the hope that it would prevent the formation of paracardial adhesions, but whereas the initial arrest of the disease was achieved, the fibrotic end-result was not influenced. In 3 cases of tuberculous peritonitis with ascites laparoscopy when the drug had been withdrawn showed fluid to be still present in only one case, but in the other two there was evidence of early adhesion formation and a thickening of the hepatic capsule. Observations made during the treatment of this series indicated that cutaneous allergy varies with the amount of ACTH given, and indeed it disappeared completely in one patient. It is claimed that there is no danger of the reactivation or spread of tuberculous lesions in the lung tissue with ACTH, provided antibiotics are given at the same time. *Thomas Marmion*

57. **Unilateral and Bilateral Bronchography with Tracheal Anaesthesia in Open Tuberculosis of the Lungs.** (Die ein- und doppelseitige Bronchographie in Endotrachealnarkose bei offener Lungentuberkulose)
W. MAASSEN. *Schweizerische Zeitschrift für Tuberkulose* [*Schweiz. Z. Tuberk.*] **11**, 427–438, 1954. 4 figs., 34 refs.

The author describes a method of bronchography in patients with active pulmonary tuberculosis which he has used successfully at Holsterhausen Sanatorium, Essen-Heidhausen. After premedication with atropine and phenothiazine [a substance now considered in Great Britain to be too toxic for use in human subjects] the patient is given an intravenous injection of one of the barbiturates producing general anaesthesia of short duration. As soon as the patient is unconscious he is given a further small quantity of the drug, followed by 60 to 80 mg. of succinylcholine chloride. During this time the patient has been breathing pure oxygen. After intratracheal intubation hyperventilation is produced with pure oxygen and reabsorption of carbon dioxide in a closed circuit. The hyperventilation results in apnoea, which may last up to 5 minutes. The patient is then placed in the appropriate position for bronchography and a water-soluble contrast medium is injected through the intratracheal tube, but filling of the alveoli with contrast medium must be avoided. As soon as the introduction of the medium is completed, a further small quantity of the relaxant is injected and unilateral or bilateral bronchography carried out. The patient is then placed in the Trendelenburg position, the contrast medium is aspirated, and an injection of lobeline given. Prophylactic doses of penicillin and streptomycin are given 4 hours before the examination and are continued for 3 days after it.

The author has employed this method in 35 cases of open tuberculosis and in 7 cases of non-specific pulmonary lesions without any harmful results, the procedure in all cases being well tolerated. Some of the main indications for this are: exploratory bronchography in doubtful cases, in poor-risk patients with emphysema, asthma, or silicosis, in cases of lobar atelectasis or rigid pneumothorax, and in patients who have recently undergone bronchoscopy. *A. Orley*

EXTRA-RESPIRATORY TUBERCULOSIS

58. **The Treatment of Tuberculous Meningitis with Isoniazid.** (Le traitement de la méningite tuberculeuse et l'I.N.H.)
R. DEBRÉ, H. E. BRISSAUD, S. A. KAPLAN, H. NOUFFLARD, J. RAYNAUD, and M. NAVEAU. *Presse médicale* [*Presse méd.*] **63**, 41–44, Jan. 12, 1955. 31 refs.

During the period 1952–3 isoniazid was used to treat 171 patients with tuberculous meningitis at the Hôpital des Enfants-Malades, Paris, of whom 143 (85%) survived, with a minimum period of observation of 6 months. In a previous series of 309 cases treated between 1947 and 1952 without isoniazid 185 patients (60%) survived. The patients in the earlier series received prolonged intramuscular and intrathecal streptomycin treatment; increasing experience from year to year did not lead to improvement in the survival rates until the advent of isoniazid. When isoniazid became available a number of patients were already under treatment with streptomycin and PAS, but only those 29 patients were given isoniazid whose progress on the previous treatment was not fully satisfactory. The 171 cases treated with isoniazid are therefore weighted with a small group of 29 in which the initial prognosis was poor. Nine of these 29 children died. The prognosis for children treated with isoniazid in combination with streptomycin and PAS from the outset was much better. Of 27 such children treated in 1952, 26 survived, and of 85 treated in 1953, 73 survived.

Of the 12 patients treated in 1953 who died, 8 were under 2 years of age, and all 4 over that age were in coma on admission. The other 58 children over 2 years of age all survived, but the prognosis for infants has not improved, only 15 of 23 having survived, death usually occurring less than 6 weeks after admission. With isoniazid treatment the majority of patients who are in coma on admission survive, but with frequent and serious sequelae; early diagnosis is therefore still essential.

During 1953 the amount of intrathecal streptomycin treatment was gradually reduced, and towards the end of that year 6 patients received very little intrathecal treatment with favourable results.

The superiority of isoniazid over streptomycin lies in its ease of administration, lack of toxicity over a wide range of therapeutic dosage, and its easy diffusibility into the cerebrospinal fluid (C.S.F.) after oral administration. However, a brief review of some of the world literature [mostly Continental] did not satisfy the authors that the omission of streptomycin from treatment is justified, and they quote two of their own cases in which isoniazid-resistant tubercle bacilli were recovered from the C.S.F.

They do not consider it possible at present to devise a scheme of treatment which is applicable to all cases. For infants under 2 years of age and for all patients with any degree of disturbance of consciousness they now use a combination of isoniazid, streptomycin, and PAS, giving daily intrathecal treatment with streptomycin and isoniazid until definite improvement has occurred. The dose of isoniazid recommended is 15 to 30 mg. per kg. body weight daily, given by mouth. For early cases in children over 2 years of age they give only PAS and isoniazid by mouth, omitting all streptomycin and all intrathecal therapy. The duration of treatment is a minimum of 8 months for all cases. Early results are said to be favourable. *John Lorber*

59. **Tuberculous Meningitis Treated with Cortisone**
M. ASHBY and H. GRANT. *Lancet* [*Lancet*] **1**, 65–66, Jan. 8, 1955. 11 refs.

At the Whittington Hospital, London, 12 adult patients suffering from tuberculous meningitis were given streptomycin intramuscularly and isoniazid by mouth for 6 months and streptomycin intrathecally for 3 to 5 months. In addition, 6 of the 12 were given cortisone by mouth in doses of 100 mg. daily for the duration of intrathecal therapy.

Of the 6 patients treated without cortisone, one died, 2 developed neurological sequelae (1 deaf, 1 blind), and one, who had been admitted with hemiplegia, remained hemiplegic after recovery. All the 6 treated with cortisone survived without sequelae except for one who suffered impairment of vision. (None of these patients had hemiplegia on admission.) Clinical improvement was more rapid in the group treated with cortisone, and the cell count of the cerebrospinal fluid fell and its sugar content rose at an earlier stage.

The authors consider that it is safe to use cortisone in the treatment of tuberculous meningitis so long as adequate antibiotic cover is provided; they also consider that intrathecal streptomycin treatment is still desirable. They claim that although their results are not conclusive, there is sufficient evidence of the beneficial effect of the addition of cortisone to the treatment of tuberculous meningitis to merit further trial.

[The authors were unfortunate with the sequelae in their first 6 cases—in larger series such sequelae are now quite rare. Further, the differences between these two small groups are less striking if one remembers that one of the first 6 had presumably irreversible hemiplegia on admission, that in the one case of deafness development of a spinal block had necessitated daily cisternal puncture for 6 months, and that the period of observation of the second group was much shorter.] *John Lorber*

60. **The Results of Treatment of Tuberculous Meningitis in Adults. A Study of 255 Cases.** (Résultats du traitement de la méningite tuberculeuse de l'adulte. Etude sur 255 cas)
E. BERNARD, A. DUROUX, A. LOTTE, A. JARNIOU, R. BOUVIER, and D. AZORIN. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **70**, 1118–1127, Nov. 26, 1954. 2 figs.

The results are reported of the treatment of tuberculous meningitis in 255 patients, four-fifths of whom were between 15 and 29 years of age, the rest being older. The first 119 patients were treated between 1947 and 1949 with streptomycin alone, and only 27 (23%) survived. The next group of 82 patients were treated between 1949 and 1952 with streptomycin and PAS, and 38 (46%) survived. The remaining 54 patients were treated in 1952 or 1953 with isoniazid (5 to 10 mg. per kg. body weight daily) by mouth, streptomycin (or dihydrostreptomycin) (1·0 to 1·5 g. daily) intramuscularly, and PAS (15 g. daily) by mouth or intravenously for some 7 months. Daily intrathecal injections of streptomycin (50 mg.) were given, often associated with isoniazid (20 mg.). Most patients received 60 or more intrathecal injections, but more recently the number of injections has been reduced. Of this group, 49 patients (93%) have survived after a minimum of one year of observation; in the authors' experience death after the first year is exceptional.

In all 3 groups the prognosis was best in early cases, whereas of 8 patients in the third group who were in coma on admission, 4 died. The unfavourable prognostic significance of associated miliary tuberculosis was no longer evident after the introduction of isoniazid.

Six of the 49 survivors in the third series have neurological sequelae, while in addition 7 are partially and 6 totally deaf (mostly due to dihydrostreptomycin). The authors are in favour of prolonged combined treatment, including the intrathecal administration of streptomycin with or without isoniazid. *John Lorber*

61. **Under What Conditions May Intrathecal Treatment be Omitted from the Treatment of Tuberculous Meningitis in Children?** (A quelles conditions peut-on se dispenser d'un traitement intrarachidien dans la méningite tuberculeuse de l'enfant?)
J. FOUQUET, V. HEIMANN, L. TEYSSIER, and —. CAYLA. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **70**, 1127–1138, Nov. 26, 1954. 14 refs.

The authors have previously reported (*Bull. Soc. méd. Hôp. Paris*, 1954, **70**, 360; *Abstracts of World Medicine*, 1954, **16**, 458) their very favourable experience in the treatment of tuberculous meningitis with isoniazid, PAS, and streptomycin, 53 patients surviving out of 57 treated.

Since in several of these cases relapse of the meningitis occurred after the discontinuation of the intrathecal treatment and while the patient was still receiving isoniazid by mouth, the process being reversed by further intrathecal treatment, they formed the opinion that it was unwise to abandon treatment by this route. More recently, however, they decided to try the effect of giving very large doses of isoniazid (40 to 50 mg. per kg. body weight) by mouth without intrathecal injections.

This was first tried in the case of a 3-year-old child who had developed bacteriologically proven tuberculous meningitis 3 months after the beginning of treatment with isoniazid and streptomycin for primary tuberculosis, when he was still receiving 10 mg. of isoniazid per kg. by mouth. Nevertheless, increasing the dose of isoniazid to 40 mg. per kg. (the additional dosage being given in the form of suppositories) led to recovery without intrathecal treatment. In 2 other cases good progress was made without intrathecal treatment, but for more advanced cases the authors still advocate intrathecal treatment, which is also given if a patient cannot tolerate the high dosage of isoniazid by mouth.

Sequelae are becoming less common, the incidence of paralysis being about 4% and of blindness 3%, while deafness no longer occurs. Severe mental retardation occurs in infants with gross hydrocephalus, but behaviour disorders are uncommon. Since the authors' previous report they have treated 12 further patients, only one of whom has died.

(In the discussion which followed the presentation of this paper Perrault drew attention to the dangers of high isoniazid dosage, especially from its antagonistic effect on vitamin B_6, which should be given in doses of 50 to 100 mg. daily to prevent toxic complications.)

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The authors report the treatment of 11 cases of tuberculous meningitis exclusively with isoniazid, which was given intrathecally in only one case. All the patients have survived, the period since the conclusion of treatment ranging from 4 to 27 months. Treatment lasted for 4 to 18 months, and in no case did the dose of isoniazid exceed 6 mg. per kg. body weight daily.

The authors challenge the logic of combined antibiotic treatment, pointing out that the sensitivity of bacteria to antibiotics under the artificial conditions of the laboratory is not necessarily identical with their sensitivity in the human body, and in any case authentic reports of the recovery of resistant organisms in cases of tuberculous meningitis are exceptional. They prefer to use different drugs successively rather than concurrently, and believe that this method conserves the full potentiality of each.

[This paper is of challenging interest, but the authors have failed to give proof of the diagnosis of their cases and other details necessary for judgment of their claims. In any case, to draw dogmatic conclusions from so few cases is unjustifiable. The presentation of the paper provoked much discussion, most of the contributors to which disagreed with the authors. It was generally conceded that with the advent of isoniazid it has been possible to reduce considerably the amount of intrathecal treatment, but the authors' rejection of combined treatment received no support. No doubt a large proportion of cases—perhaps as many as 80%—could be cured with oral isoniazid alone, but, as Marquezy pointed out, this figure can be increased to 97% by the addition of streptomycin.]

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The author reports from the Municipal Dermatological Clinic, Gera, Germany, that of 80 patients with tuberculous cervical adenitis all were treated conservatively with good results. In 52 cases the condition was one of simple adenitis, but in 28 it was complicated by fistula; 48 of the patients were under 14 years of age. After a full investigation, in which particular care was taken to discover if there were tuberculous foci elsewhere in the body, the patient was given isoniazid in a dose of 5 or 6 mg. per kg. body weight, together with 100,000 units of vitamin D_2 six times weekly for one month, after which time the dose was gradually decreased. Liquefying nodes were aspirated and isoniazid injected. In 33 cases the adenoids or tonsils were removed a week or two after the onset of treatment, as it was found that they were commonly the seat of the primary infection.

It is stated that 23 patients (12 under the age of 14) were completely cured, 53 were "improved" or "greatly improved", and only 4 did not benefit from the treatment.

In the author's opinion surgical excision with radiotherapy is bad practice in the treatment of these cases.

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The author stresses the importance of considering a diagnosis of tuberculous mesenteric adenitis in children with unexplained abdominal pain and fever, and points out that calcification does not signify a healed lesion, which may be disregarded as a cause of symptoms.

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The author considers this form of therapy particularly valuable in the case of children, in whom ankylosis can often be avoided by the early intra-articular administration of antibiotics and antituberculous drugs. It is emphasized, however, that in cases in which other forms of treatment have been given previously the value of intra-articular therapy is greatly diminished.

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Progress in the treatment of genito-urinary tuberculosis in a special unit of 35 beds at Wrightington Hospital, Lancashire, is reviewed in the light of the findings at follow-up investigation in 155 cases treated between 1949 and 1952 and the results obtained in 85 patients treated since July, 1952.

It is first pointed out that the prognosis in genito-urinary tuberculosis has greatly improved as a direct result of the use of chemotherapeutic drugs in combination with surgery; up to 1950, when the treatment of this disease was by surgery and sanatorium care only, mortality was about 50%; since that date mortality has fallen to 10%. Surgery is as necessary as ever, but should not be carried out until the patient has received adequate chemotherapy, which, in the authors' unit, consisted in an intramuscular injection of 2 g. of streptomycin and 250 mg. of isoniazid by mouth daily for 14 days, followed by 100 to 150 mg. of thiosemicarbazone daily and 7 g. of calcium benzoyl PAS three times a day also for 14 days, these combinations alternating for a period of 6 months.

As a result of this additive treatment there have been three notable improvements in the type of operation it is possible to perform and in the results achieved: (1) ulcerocavernous lesions in one pole of a kidney can be treated by partial nephrectomy, thus permitting surgery of bilateral lesions (though this type of lesion in the kidney still does not heal with chemotherapy alone); (2) epididymectomy can be carried out alone in nearly all cases of tuberculous epididymitis; and (3) breaking-down nephrectomy wounds are no longer encountered.

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[This paper should be consulted in the original by those interested, as it gives a great deal of information on the results of the various surgical procedures employed.] *F. B. Cockett*

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The authors describe the treatment at the Forlanini Institute, Rome, of 21 cases of miliary and generalized pulmonary tuberculosis in children ranging in age from 2 to 12 years. The patients were subdivided into two groups, 11 being treated either with intramuscular injections of dihydrostreptomycin alone or with this drug in combination with PAS, and the remaining 10 patients with dihydrostreptomycin and isoniazid. The authors found that the latter combination gave better results than did streptomycin alone or streptomycin and PAS. In all 10 cases in the second group the duration of the disease was reduced, there was complete clinical and radiological recovery, and no toxic side-effects from streptomycin were observed. Details of dosage and brief case histories are given. In the first group 2 patients died and one was removed from the clinic before completion of treatment. *Franz Heimann*

Venereal Diseases

69. **Quantitative Studies of Ageing Sera in the Wassermann Reaction with Cardiolipin.** (Quantitativ Auswertung alternder Wa.R.-Sera mittels Cardiolipin)
H. RUGE. *Zeitschrift für Hygiene und Infektionskrankheiten* [*Z. Hyg. InfektKr.*] **140**, 521–527, 1955. 5 refs.

At the University Skin Clinic, Erlangen, 940 samples of syphilitic serum were tested by means of the Wassermann reaction using cardiolipin antigen, and then, after being kept for various periods, were re-tested two or more times at intervals of 4 to over 30 days; 60 samples were examined on 4 or more occasions, the rest less often. A significant and progressive fall in the titre was observed with the ageing of the sera. Differences of 3 or more dilutions were more frequent in specimens obtained from patients with active late syphilis. The effect of treatment was also to produce a larger fall in the titre with ageing. The factors responsible for this phenomenon are not known.

[The detailed results are tabulated and do not lend themselves to abstracting.] *G. W. Csonka*

70. **The Fundamentals of Penicillin Therapy in Syphilis.** (Las bases de la penicilinoterapia en la sifilis)
T. GUTHE. *Actas dermo-sifiliográficas* [*Act. dermo-sifiliogr. (Madr.)*] **46**, 159–175, Dec., 1954. 3 figs., bibliography.

The author, who is head of the Section for Venereal Diseases and Treponematoses of the World Health Organization (W.H.O.), outlines the fundamentals of the treatment of syphilis by modern methods. A 6-year follow-up study of the results obtained in the treatment of secondary syphilis with penicillin alone and with penicillin in combination with arsenic and bismuth has shown that no additional benefit results from the addition of metal therapy. Moreover, penicillin is also safer, easier to administer, and much cheaper. In the author's experience the Herxheimer reaction is not to be feared except sometimes in the treatment of the newborn. The new long-acting penicillins now available make possible the adequate treatment of syphilis in one or at the most a few injections, whereas because of the prolonged course necessary with arsenic and bismuth only some 10% of patients completed treatment. A world survey carried out by W.H.O. showed that some 63% of venereologists use penicillin alone in the treatment of syphilis.

The author goes on to stress the importance of the time factor in treatment with penicillin, pointing out that the blood concentration of the antibiotic should never be allowed to remain for long below treponemicidal levels during treatment. The time required by the treponeme for multiplication is about 30 hours, so that the period during which the blood level is below 0·03 unit of penicillin per ml. of serum should not last longer than 24 hours. In seronegative cases of primary syphilis as little as 4 days' treatment with penicillin may suffice, and the results of therapy are not improved by prolonging it for more than 14 days, nor by inducing high blood concentrations of the drug. A test dose of 300,000 units of P.A.M., as recommended by W.H.O., should produce a level of 0·03 unit of penicillin per ml. of serum for a period of 72 hours. The following dosage schemes are suggested: (1) 300,000 or 600,000 units of P.A.M. given daily or on alternate days to the total dosage required; (2) injections of 1·2 or 2·4 mega units of P.A.M. at longer intervals corresponding to the size of the dose; or (3) a single injection of between 4·8 and 6 mega units of P.A.M. The use of abortive and prophylactic treatment with penicillin is discussed and is recommended for the consorts of patients with infectious syphilis and for the contacts of cases of endemic syphilis and yaws. In conclusion the author points out the danger of producing resistance to penicillin by giving the drug by mouth or parenterally in comparatively small doses for trifling infections. Up to the present, however, there has been no evidence that treponemes are becoming resistant to penicillin. *Eric Dunlop*

71. **Prolonged Reaction to Intramuscular Benzathine Penicillin**
H. C. ANDERSON. *Lancet* [*Lancet*] **2**, 1157–1158, Dec. 4, 1954. 1 fig., 9 refs.

72. **Incidence of Corneal Changes in Congenital Syphilis**
E. M. C. DUNLOP and F. B. ZWINK. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **30**, 201–209, Dec., 1954. 5 figs., 21 refs.

Of a series of 117 patients aged 5 to 70 years with congenital syphilis examined at the Whitechapel Clinic of the London Hospital with the slit-lamp corneal microscope, 74 (63%) showed undoubted evidence of interstitial keratitis, past or present. None of 14 patients in whom the diagnosis was probable but not certain showed corneal changes. If the two groups are taken together the incidence of corneal change was 56%, while if those patients who attended the clinic primarily on account of interstitial keratitis are excluded the incidence was 44%. Of the 74 patients with evidence of interstitial keratitis, both corneae were involved in 63 (84%). A history of misty vision lasting for more than a few days was the most important single symptom in the diagnosis of former interstitial keratitis: macroscopical examination of the eye was frequently misleading.

It is considered desirable that all patients in whom the diagnosis of congenital syphilis is probable or certain should be examined with the slit-lamp microscope. In the authors' series corneal microscopy played an important part in amending the diagnosis of one in ten of all the cases reviewed. *R. R. Willcox*

73. **Late Congenital Syphilis of the Inner Ear—a Sequel of Chronic Osteomyelitis of the Petrous Bone.** (Die Lues hereditaria tarda des Innerohres—eine Folge chronischer Osteomyelitis des Felsenbeins)
F. R. NAGER. *Practica oto-rhino-laryngologica* [*Pract. oto-rhino-laryng.* (*Basel*)] **17**, 1–22, 1955. 8 figs., 24 refs.

In cases of late congenital syphilis chronic middle-ear disease is a common occurrence. Deafness, resulting from changes in the perceptive apparatus, may occur secondarily as a consequence of spread from the middle ear (tympanogenic). A sero-fibrinous labyrinthitis or a syphilitic osteomyelitis may be produced.

In this paper from the University Ear Clinic, Zürich, the author reviews a number of such cases reported in the literature, especially with regard to the histological findings, and adds 2 cases of his own in which progressive deafness of inner-ear type was noticed and in which the petrous bones were subsequently examined microscopically post mortem. In one case, in which death was due to miliary tuberculosis, the middle ear was quite normal and the main changes were those of a labyrinthitis. In the second the changes were characteristic of a syphilitic osteitis with chronic inflammatory changes in the middle ear which, however, had not affected the bone directly. In this case an otosclerotic focus was noticed on one side. It is suggested that the bone changes may, in some of these cases, be the result of a haematogenous spread, and it is considered that the histological pictures in the two cases described represented two different stages in the same disease process. *G. E. Stein*

74. **Congenital Syphilis. A Follow-up Study with Reference to Mental Abnormalities.** [In English]
B. HALLGREN and E. HOLLSTRÖM. *Acta psychiatrica et neurologica Scandinavica* [*Acta psychiat. neurol. scand.*] Suppl. 93, 1–81, 1954. Bibliography.

75. **Late Congenital Neurosyphilis (General Paresis and Tabes).** (Neurosífilis congénita tardía. Parálisis general juvenil—tabes juvenil)
M. ARNDT and A. F. THOMSON. *Acta neuropsiquiatrica Argentina* [*Acta neurosiquiat. argent.*] **1**, 3–42, Oct., 1954. 7 figs., bibliography.

An account is given of 20 cases of late congenital parenchymatous neurosyphilis (16 of general paresis and 4 of tabes dorsalis) seen between 1940 and 1954 at the Buenos Aires Institute of Neurological Research. In only 12 cases was it possible to diagnose syphilis in the parents, only 3 of whom themselves showed signs of neurosyphilis.

The 16 congenital cases constituted 1·8% of a total of 877 cases of general paresis seen during this period. The psychiatric picture was of dementia which either started at a very early age as a generalized mental deficiency or developed during late childhood (average age 13·9) in an apparently normal child. In the latter group a catatonic or depressive picture was observed at the onset. Pupillary abnormalities were present in all cases, inequality and abnormal responses to light being the most frequent. Speech disturbances were present in all but one patient, speech being slow, monotonous, and slurred in the initial stages, then gradually becoming explosive, repetitive, and more and more inarticulate and unintelligible until mutism finally developed. An intense or partial optic atrophy was found in 9 cases. Tremor of the hands and tongue was present and was similar to that of the acquired form. Hyperactivity and motor restlessness were common. The tendon reflexes were reduced in 5 cases and increased in 9, an extensor plantar response being present in one case only. Fits occurred in 6 cases, one patient having up to 20 daily. The cerebrospinal fluid showed changes which did not differ from those found in adult paretics. On the whole these juvenile cases responded very poorly to malaria and penicillin.

The 4 cases of tabes are also described in detail. The onset was at puberty, except in one case in which it was delayed until the age of 34. The clinical picture differed in no way from that of the acquired form.
Richard de Alarcón

76. **The Relationship between Clinical and Electroencephalographic Findings in General Paresis.** (Correlaciones clínico-electroencefalográficas en la parálisis general progresiva)
A. MOSOVICH and G. WEICKHARDT. *Acta neuropsiquiatrica Argentina* [*Acta neuropsiquiat. argent.*] **1**, 43–60, Oct., 1954. 5 figs., 15 refs.

A comparative study of the electroencephalographic and clinical features of 20 cases of dementia paralytica was made at St. Elizabeth's Hospital, Washington, D.C. The patients ranged in age from 28 to 58. None suffered from epileptic fits, and the diagnosis was fully confirmed by neurological and laboratory findings. The time of the primary infection was unknown in most cases. Six patients showed progressive dementia, 11 a megalomanic picture, 2 depressive features, and 2 anxiety and homicidal tendencies.

The electroencephalograms (EEGs) before treatment were classified as follows: 4 normal, 4 "slightly abnormal", 7 "moderately abnormal", and 5 "frankly abnormal". Of the patients in the last two groups, 5 showed predominant slow frontal activity and 2 mixed frontal delta and fast rhythms. In 12 cases there was an abnormal response to hyperventilation, with generalized paroxysmal phenomena and greater slowing in the frontal leads. The most common abnormalities were frontal slow activity and cortical instability revealed by a dysrhythmic response to hyperventilation. No correlation was found between the EEG and the neurological and psychiatric picture. A slight improvement in the EEG was observed in some cases after treatment, but it was not significant or conclusive. There was, however, a correlation between the initial EEG and the response to treatment, patients with a normal or near normal initial record responding much better to penicillin and malaria. *Richard de Alarcón*

77. **Use of Streptomycin to Combat Contamination of *Treponema pallidum* Suspensions in the TPI Test**
R. K. LEDBETTER and R. J. CUMMING. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **30**, 214–215, Dec., 1954. 1 fig., 5 refs.

Tropical Medicine

78. **The Diagnosis of Onyalai**
J. WILKINSON. *East African Medical Journal* [*E. Afr. med. J.*] **31**, 549–556, Dec., 1954. 14 refs.

The author presents a comprehensive review of onyalai, which is a haemorrhagic disease similar to thrombocytopenic purpura and characterized particularly by blood blisters on the tongue, mucous membranes, and skin. It affects mainly young adults of the Bantu race, among whom it is more common in males than in females. Cases have been described, however, in other races—European (6 out of 354 reported cases), Hottentot, and Chinese. The disease was thought to be confined to lands south of the equator in Africa, but recently cases have been reported in Kenya, Nyasaland, and Eritrea. Clinically, the blood blisters are pathognomonic; they occur typically on the tongue, where they may be up to 1 cm. in diameter, are dome-shaped and pink at first, and later may show umbilication and become bluish or black. After discharging their contents they become painful, circular, shallow ulcers which quickly heal. Blisters also occur on the buccal mucosa and skin. Bleeding is a prominent symptom, particularly epistaxis and bleeding from the gums, but haemorrhages from the bowel, vagina, and bladder have also been described. Purpura in the skin and subconjunctival haemorrhage have been noted in some cases. Intracranial haemorrhage is common and usually fatal; this is the only type of haemorrhage involving a vital organ so far described.

The blood picture is that of a secondary anaemia if haemorrhage has been severe. Reduction in number of the platelets is an inconstant finding. Coagulation time is normal, bleeding time prolonged, and clot retraction poor. In mild cases constitutional symptoms are generally absent, but when present are similar to those of any febrile illness. A characteristic symptom is aching in the region of the parotid glands. In the differential diagnosis scurvy, some kinds of snake-bite, and secondary thrombocytopenic purpura have to be considered. The history of the case and the tell-tale blood blisters in characteristic sites should make diagnosis simple. It is hoped that a knowledge of these diagnostic features will lead to wider recognition of the disease, which is probably more widespread than has been thought. *William Hughes*

79. **Daraprim as a Malaria Suppressant**
D. H. S. ANNECKE and A. J. JACOBS. *East African Medical Journal* [*E. Afr. med. J.*] **31**, 543–547, Dec., 1954. 7 refs.

The authors present results of a test of " daraprim " (diaminopyrimidine; pyrimethamine) as a malaria suppressant in native African children aged from 2 to 7 years living in villages on the Klein Letaba River in Northern Transvaal, where *Anopheles gambiae* is the vector. In this area the rainfall is usually low (12 to 15 inches (30 to 38 cm.) per annum) and mosquito density was also low during the experimental period, the count of female adult anophelines being never more than 2 per hut. Dissection of 100 females yielded mature cysts in the stomach of 2 and sporozoites in the salivary glands of one. Daraprim was given in a dosage of 12·5 mg. weekly, one dose a month being given by the authors themselves, the other three being left to the parents to administer, which there was good reason to think they did. The trial lasted 6 months, from November, 1953, to April, 1954, and 52 children were treated, 48 others of similar age and circumstances acting as controls.

In the treated children the parasite rate fell from 74·1% to *nil* and the spleen rate from 48·5 to 5·4%; in the controls the parasite rate fell from 81 to 43%, while the spleen rate rose from 42 to 62%. The gametocyte rate, which was 15% before treatment in both groups, fell to *nil* in the treated group, but did not fall below 8% in the controls during the period of the trial. Five weeks after cessation of treatment the parasite rate had risen to 21%, the spleen rate to 9%, and the gametocyte rate to 2% in the treated group, indicating that the suppressive action of the drug had not eradicated the parasite.

The authors are satisfied that suppressive daraprim treatment would be useful in certain special circumstances, but in their opinion the difficulties of administration, the quick relapses, and the possibility of developing resistant strains do not encourage its general use in native populations. *William Hughes*

80. **The Susceptibility of Fourth-stage Larvae of *Anopheles gambiae* to Oil Solutions of DDT and Dieldrin under Semi-natural Conditions**
G. WEBBE. *East African Medical Journal* [*E. Afr. med. J.*] **32**, 41–45, Feb., 1955.

81. **Ineffectiveness of DDT Residual Spraying in Stopping Malaria Transmission in the Jordan Valley**
M. A. FARID. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **11**, 765–783, 1954.

The malaria control campaign by residual spraying with DDT which has been carried out in the valley of the River Jordan is reviewed. In the narrow northern part of the valley, where the river is sinuous, with many backwaters, and the villages are seldom far from the river, malaria is a special problem. Some of the inhabitants live in houses, but many are " tent-dwellers " often sleeping in the open.

Between 1949 and 1951 houses and tents were sprayed with DDT, leaving a residual film, but there was no reduction in the incidence of malaria, although the domestic vector, *Anopheles sacharovi*, was almost eliminated from sprayed premises. In 1951 large

numbers of *A. superpictus* and *A. sergenti* were found in caves and fissures of the near-by sandstone hills, and an effort was therefore made in 1952 to control malaria by spraying caves. No diminution in the incidence of malaria was noted, but the failure was not attributed to the brand of DDT used, since it had already been found that sprayed premises were almost free from mosquitoes whereas unsprayed control premises were not. Close observation indicated that the mosquitoes attacked the inhabitants at night in the open, the daytime-resting and the breeding places of the *Anopheles* being caves and fissures in the hills. Thus there is still a high rate of malaria transmission in the Jordan valley in spite of the residual spraying campaigns carried out since 1949, and it is concluded that if malaria is to be controlled in this area antilarval measures must be resumed.

W. H. Horner Andrews

82. **Extension to Chlordane of the Resistance to DDT Observed in *Anopheles sacharovi***

G. D. GEORGOPOULOS. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **11**, 855–864, 1954. 3 figs., 4 refs.

In 1952 in the Skála district of Lakonia, Peloponnese, where spraying with DDT had been in progress for 5 years, it was found that the local malaria vector, *Anopheles sacharovi*, had developed some resistance to both DDT and " gammexane ". It was noted, however, that under laboratory conditions in the same area chlordane and dieldrin were lethal to 100% of *A. sacharovi*.

In July, 1952, all houses and stables in the village of Leimonas (except 3 stables used for control purposes) were sprayed with a 74% emulsion of chlordane to give a concentration of 1·5 g. per square metre. After 5 days mosquitoes were collected daily from sprayed premises, from unsprayed stables, and also from stables in the unsprayed village of Souli 4 miles (7 km.) away. The collected mosquitoes were transferred to large cages and the number of dead counted after 24, 48, and 72 hours. The survival rate of the mosquitoes caught inside sprayed premises was almost the same as that of mosquitoes caught in unsprayed premises and in the distant unsprayed village, indicating some resistance to chlordane. The proportion of dead *Anopheles* in a 24-hour catch reached a maximum 20 days after spraying and was under 40%; the control figure was less than 5%.

W. H. Horner Andrews

83. **Evidence of the Development of Resistance to DDT by *Anopheles sacharovi* in the Levant**

C. GARRETT-JONES and G. GRAMICCIA. *Bulletin of the World Health Organization* [*Bull. Wld Hlth Org.*] **11**, 865–883, 1954. 3 figs., 8 refs.

The authors report an investigation of the resistance to DDT of *Anopheles sacharovi* in certain areas in north Lebanon near the Syrian border. In 1953, 18 months after the start of residual spraying with DDT, resting *A. sacharovi* reappeared on treated walls. The mortality within 48 hours of female mosquitoes having a known minimum contact of 5 to 15 minutes with DDT residues (estimated at 0·1 to 2·0 g. per square metre) was 45·1% to 60·1%, according to the technique used. In similar tests performed some months earlier on the same strains mortality after 24 hours was 83 to 100%.

It thus appeared that resistance to DDT had developed after spraying had been in operation for two seasons only, though some spraying had been carried out sporadically in certain areas. The premises sprayed varied from rough stone houses to mud-lined huts " composed of cane and maize-straw mats ". Inside walls in both types of dwelling tended to become covered with soot from charcoal cooking fires, and it is suggested that the surface of the walls absorbed the DDT residue, thus reducing the level below the critical range for the mosquito.

The techniques used in assessing resistance and the local behaviour of the *Anopheles* are described. Although some resistance developed, the incidence of *A. sacharovi* during the second season of spraying was found to be much lower in the treated than in the untreated premises.

W. H. Horner Andrews

84. **Control of *Ornithodoros moubata* (Murray) by Gammexane**

R. B. HEISCH and M. FURLONG. *East African Medical Journal* [*E. Afr. med. J.*] **31**, 561–562, Dec., 1954. 5 refs.

The authors describe the use of " gammexane " (gammabenzene hexachloride) for the eradication of the tick *Ornithodoros moubata* (Murray), which is the host of the spirochaete causing relapsing fever. In treating native huts in Kenya two preparations were used. A gammexane insect powder containing 0·5% gamma isomer was dusted over the floors and a little way up the walls in a concentration of about 4 lb. per 1,000 sq. feet (2 kg. per 100 sq. m.) of surface; the second preparation was a gammexane wettable powder (" P.520 "), 12 oz. (340 g.) of this added to one gallon (4·5 litres) of water being used to spray 1,000 sq. feet (93 sq. m.), including the earthen floor and the walls up to a height of 18 inches (45 cm.).

In the first trial 15 huts were chosen, 10 being treated with P.520 and 5 left as a control. In the treated huts ticks were rapidly reduced in numbers and had almost disappeared 5 weeks later; they began to reappear, however, 11 weeks after treatment. After a second spraying the treated huts remained free for a further 8 months. In the second trial, made in December, 1952, 30 huts were chosen, 10 being treated with gammexane insect powder, 10 with wettable gammexane, and 10 acting as controls. Here again P.520 eliminated the ticks, whereas the gammexane powder reduced the number of ticks but did not eliminate them. A second application of P.520 was made in the following April (1953), this time all 30 huts together with 136 intervening dwellings being sprayed. Re-examination after 8 months showed that only 2 of the 30 huts were re-infested.

The authors consider that the trial demonstrates the advantages of repeated as against single applications of insecticide, and conclude that P.520 used as a spray is much more effective than the gammexane powder in previous use.

William Hughes

Allergy

85. **Skin Allergy to Simple Gaseous Sulphur Compounds.** [In English]
V. PIRILÄ. *Acta allergologica* [*Acta allerg.* (*Kbh.*)] 7, 397–402, 1954. 1 fig., 11 refs.

From the Institute of Occupational Health, Helsinki, a case of urticaria due to sulphur dioxide and one of dermatitis due to hydrogen sulphide are described. It is stressed that simple gaseous sulphur compounds present as air contaminants in industrial centres may on rare occasions cause skin rashes in sensitized persons.
A. W. Frankland

86. **Corticotrophin, Cortisone, and Hydrocortisone in Diseases of Hypersensitivity. I. Biological Corticoid Excretion during Acute Symptoms**
B. ROSE, T. W. FYLES, and E. H. VENNING. *Journal of Allergy* [*J. Allergy*] **26**, 1–10, Jan., 1955. 7 figs., 23 refs.

In 58 cases of chronic asthma (29 in males, 29 in females) studied at the McGill University Clinic, Royal Victoria Hospital, Montreal, urinary glucocorticoids were assayed by the method of Venning, Kazmin, and Bell, in which the results are expressed in glycogen units, one unit being equivalent in activity to 1 μg. of cortisone. During attacks the corticoid excretion of the asthmatics did not differ significantly from the average normal figures given by Venning *et al.*, although it was somewhat reduced in the male patients. However, when those patients with severe asthma who needed continuous treatment and were difficult to control were considered separately it was found that their glucocorticoid excretion was below normal [but it is not mentioned whether these patients, as is likely, received adrenaline-like drugs during their attack, which may have influenced the result].

In one case of spontaneous recovery from an asthmatic attack glucocorticoid excretion increased during recovery. In another case glucocorticoid excretion increased steeply during an 8-day period of fever therapy consisting in repeated injections of T.A.B. vaccine to induce bouts of high temperature. In 11 cases of allergic skin disease urinary glucocorticoid excretion did not differ from normal.
H. Herxheimer

87. **The Effect of Helium–Oxygen Mixtures on Pulmonary Function in Asthmatic Patients**
I. W. SCHILLER, F. C. LOWELL, M. T. LYNCH, and W. FRANKLIN. *Journal of Allergy* [*J. Allergy*] **26**, 11–15, Jan., 1955. 1 fig., 10 refs.

The effect on pulmonary function of the inhalation of mixtures of helium and oxygen, which has been recommended for the relief of asthma, was studied at the Massachusetts Memorial Hospitals (Boston University School of Medicine). The patients breathed successively from tanks containing atmospheric air and a mixture of 80% helium and 20% oxygen, estimations being made of the vital capacity and its subdivisions and of the expiratory volume during the first second of the vital-capacity determination, while arterial oxygen saturation was estimated with an ear oximeter. No measurement was made until the patient had been breathing the mixture concerned for at least 6 minutes. A total of 37 pairs of values were obtained from 8 patients with asthma of moderate severity, most patients with very severe asthma being unable to tolerate the test. No significant differences were found between the values obtained with air and with the helium mixture, and such small differences as were observed occurred in the less severely ill patients.

The theoretical argument for the use of helium–oxygen mixtures in asthma is based on the assumption that turbulence is a significant factor contributing to resistance to air flow. It is pointed out, however, that neither turbulence nor tissue "viscance" (resistance to deformity) is likely to be of importance in asthmatic obstruction, as both would affect expiration and inspiration equally, whereas in asthmatics expiration only is usually impaired and most patients can inhale with great rapidity.
H. Herxheimer

88. **ACTH and Cortisone in the Treatment of Asthma**
H. S. BALDWIN, P. F. DEGARA, A. D. SPIELMAN, and M. DWORETZKY. *Journal of Allergy* [*J. Allergy*] **26**, 44–53, Jan., 1955. 8 refs.

At the New York Hospital–Cornell Medical Center ACTH (corticotrophin) or cortisone was given to 60 patients with asthma who did not respond to routine treatment or were in status asthmaticus. Half of the patients received maintenance therapy with these drugs for periods up to 39 months, the others receiving them only for a short period in order to tide them over some particularly severe attack. Most of the patients were between 40 and 70, and 25 were male and 35 female.

In 52 of the 60 cases the results of treatment were satisfactory. Among the few complications observed were depression in one case and moon-face in several. No evidence of osteoporosis was seen in radiographs of bones of patients receiving large maintenance doses, and in no case did haemorrhage from a peptic ulcer occur. Seven of the patients died while under observation, but only 2 of them while receiving hormone therapy, the dosage in each case being small; both died of heart failure. In 16 cases the patient underwent some surgical procedure while under treatment; the dosage was increased during the period of the operation, and no setback occurred. In a number of cases cortisone was replaced by ACTH, and vice versa, without impairment of the beneficial effect.
H. Herxheimer

89. **Effects of 9α-Fluorohydrocortisone Acetate Administered to Patients with Asthmatic Bronchitis**
C. S. WAKAI and L. E. PRICKMAN. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **29**, 663–665, Dec. 22, 1954. 2 refs.

Nutrition and Metabolism

90. **Observations on Porphyria Cutanea Tarda**
L. A. BRUNSTING. *Archives of Dermatology and Syphilology*. [*Arch. Derm. Syph. (Chicago)*] **70**, 551–564, Nov., 1954. 5 figs., 34 refs.

Recent work on porphyria has led to the recognition of two distinct forms of the disease, the rare erythropoietic and the hepatic, the latter being again subdivided into intermittent acute porphyria and porphyria cutanea tarda, though mixed forms may occur. At the Mayo Clinic 34 cases (26 of them in males) of porphyria cutanea tarda have been seen since 1944. In most of the cases signs of the disease first appeared on the skin when the patient was between 40 and 65 years of age and remained limited to the skin. A familial incidence was not uncommon. There was an unexpectedly high incidence of diabetes mellitus and alcoholism in these patients, and functional impairment of the liver, which was observed in 25, was usually closely related to the degree of alcoholism. Hyperpigmentation of the skin was sometimes accompanied by vitiligo of the hands. There was mild blistering and scarring of exposed surfaces, with melanosis and a violaceous hue. Hypertrichosis was seen in 7 of the females. Histological examination showed a benign type of blistering and degenerative changes in the corium, but nothing characteristic. No benefit was obtained from folic acid, vitamin B_{12}, or riboflavin. Patients with porphyria cutanea tarda should avoid taking alcohol. *E. Lipman Cohen*

91. **N-Hydroxyethylethylenediamine Triacetic Acid, Versenol, in the Treatment of Hemochromatosis**
M. J. SEVEN, H. GOTTLIEB, H. L. ISRAEL, J. G. REINHOLD, and M. RUBIN. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **228**, 646–651, Dec., 1954. 1 fig., 20 refs.

N-Hydroxyethylethylenediamine triacetic acid ("versenol") forms a chelate with ferric iron which is stable in alkaline as well as in acid media, in contrast to the chelate formed with ethylenediamine tetraacetic acid (EDTA), which is decomposed by alkali. As the latter has been used with some success in cases of lead poisoning the authors hoped that the former might be effective in removing the iron deposits which are a feature of haemochromatosis. At Philadelphia General Hospital, therefore, 2 cases, one of suspected and one of confirmed haemochromatosis, were treated for short periods with versenol given as an intravenous infusion in normal saline solution.

The first case had a relatively low serum iron level and low iron-binding protein saturation and was probably not a case of true haemochromatosis. Infusion of 0·5 g. of versenol in 100 ml. of saline was given on 2 successive days but caused only a slight rise in urinary iron excretion. The second case was one of well-established haemochromatosis. A 4-day course of versenol caused a threefold increase in iron excretion on the 3rd day which was nearly fivefold by the 4th day. The iron output continued high for 3 days after treatment ceased, a total of 16 mg. of extra iron in all being excreted. The authors point out, however, that withdrawal by venesection of half a litre of blood would have removed 265 mg. of iron from the body. They conclude nevertheless that treatment with versenol may be of some value where phlebotomy is contraindicated, but at present it is much less effective than venesection. *C. L. Cope*

92. **The Treatment of Hyperpotassemia: Some Observations on the Use of a Carbonic Anhydrase Inhibitor as a Therapeutic Aid**
V. MOSELEY and N. B. BARODY. *Southern Medical Journal* [*Sth. med. J. (Bgham, Ala.)*] **48**, 1–6, Jan., 1955. 1 fig., 8 refs.

In this paper from the Medical College of South Carolina and the Roger Hospital, Charleston, the causes of a raised plasma potassium level and the clinical picture and electrocardiographic changes seen in hyperpotassaemia are first outlined. The authors then discuss some therapeutic measures, particularly the use of a carbonic anhydrase inhibitor, "diamox" (acetazoleamide). In patients with anuria such measures as administration of insulin and glucose solution, injection of hypertonic saline, and intestinal and peritoneal dialysis will generally reduce the plasma potassium level, and the authors briefly describe cases in which these measures were effective. In patients with chronic renal disease, however, the use of dialysis to lower the plasma potassium level is scarcely justified, and the authors advise administration of diamox. In 6 such cases a good response was obtained, the plasma potassium level being effectively lowered. The authors point out, however, that during treatment acidosis is likely to be increased by further depression of urinary excretion of acid, and this may require correction with sodium lactate.

[Since in chronic renal failure acidosis is more constantly observed than hyperpotassaemia this method is probably limited in application and demands close biochemical control.] *D. A. K. Black*

93. **Observations on the Aetiology of Idiopathic Steatorrhoea. Jejunal and Lymph-node Biopsies**
J. W. PAULLEY. *British Medical Journal* [*Brit. med. J.*] **2**, 1318–1321, Dec. 4, 1954. 5 figs., 22 refs.

The author describes his findings on examination of biopsy material obtained at laparotomy in 4 cases of idiopathic steatorrhoea. In all cases the villi were about double the width of those observed in control material taken from patients without steatorrhoea. Cellular infiltration of the villi was evident, mainly by plasma cells and eosinophil granulocytes. There was some evidence of oedema and the goblet cells appeared to be more prominent in the patients with steatorrhoea than in the controls. *A. C. Frazer*

Gastroenterology

STOMACH AND DUODENUM

94. **The Potentialities of the Electrogastrograph**
H. S. MORTON. *Annals of the Royal College of Surgeons of England* [*Ann. roy. Coll. Surg. Engl.*] **15,** 351–373, Dec., 1954. 16 figs., 31 refs.

The electrogastrograph is an apparatus in which silver–silver-chloride electrodes are used to record changes in potential across the wall of the stomach. The reference electrode is applied to the skin, and the other electrode, suitably protected, is passed into the stomach through the nose. After D.C. amplification the potential difference (P.D.) is recorded continuously by means of a pen-writing or hot-wire instrument on moving paper. The author discusses the genesis of bioelectrical potentials as measured in the body and the various components contributing to them, and shows that the electrogastrographic complex is made up of a steady metabolic potential probably related to the secretory activity of the mucosa, superimposed on which are small variations due to the action potentials of muscular activity. The normal electrogastrogram (EGG) shows a basal P.D. level of approximately zero (with reference to the skin), varying with the position of the electrode in the stomach between +10 mV (cardia) to −5 mV (pylorus). Characteristically, rhythmic variations in 5 frequency "bands" may be recognized. The dominant frequency is 3 cycles per minute, the waves having an amplitude of about 1 mV, representing rhythmic contractions of the gastric muscle layers. Variations at 6 to 15 cycles per minute, similar to those usually observed in the small bowel, may be recorded from the stomach after vagotomy and are associated with segmental movements. The other frequency bands in the EGG are associated with respiration, peristaltic movements, and nausea. Recordings made at operation with the reference electrode applied subcutaneously and on the serosa give P.D. levels of −35 to −50 mV (stomach to subcutaneous tissue) and −50 to −80 mV (stomach to serosa), but the basic wave patterns are similar to those recorded with the skin as reference point.

Patients with gastrointestinal disease show characteristic changes in the EGG. In gastric ulcer normal tracings are obtained if the patient lacks symptoms, as after a period of bed rest. In cases of active duodenal ulcer the EGG usually shows an increased P.D. level (up to +15 mV), with irregular, prominent spike variations and longer waves in the slow frequency band. The amount of abnormal activity in the EGG is proportional to the severity of the symptoms. Active gastric ulcer, on the other hand, is usually associated with a regular tracing with moderate increase in amplitude and with faster frequencies superimposed. While the tracing is usually normal in gastritis, in cases of acute gastric erosion (gastrostaxis) there is an increase in amplitude of the waves at 3 cycles per minute (5 to 10 mV) and a basal P.D. of 0 to 10 mV. Carcinoma of the stomach is usually characterized by irregularity of the EGG in both rhythm and amplitude; among 40 cases of proved carcinoma, only in 3 was the EGG not characteristic of the condition, while in 5 others in which the clinical and radiological diagnosis was of carcinoma but the EGG was normal the lesion was found at operation not to be malignant. In 7 cases of pernicious anaemia and achlorhydria the EGG showed an active, rather irregular pattern with a P.D. level of 20 to 30 mV.

The effects on the EGG of emotion, of electrical stimulation of the cerebral cortex (island of Reil), and of an induced epileptiform fit have been studied experimentally, the results indicating that the cortex controls the hypothalamus, which in turn affects the stomach through the autonomic nervous system. Similarly in cases of jejunitis, regional ileitis, and ulcerative colitis in which vagotomy effected symptomatic relief the EGG showed a change from increased activity to quiescence. The EGG also showed clearly the stimulant or depressing action on the stomach of certain drugs, such as atropine, methantheline, eserine, histamine, and insulin. The changes induced may affect both the P.D. level and the frequency and amplitude of the rhythmic variations. Further possible applications of the method to the investigation of gastric and intestinal function are discussed.

[This is a stimulating preliminary account, but considerable further work is required before the full clinical potentialities of the method can be assessed.]

Derek R. Wood

[An abridged version of this paper was published in the *Canadian Medical Association Journal* for December, 1954 (**71,** 546).—EDITOR]

95. **Histamine Gastric Analysis as a Screening Method in Gastric Cancer Detection**
C. W. WIRTS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229,** 1–7, Jan., 1955. 15 refs.

The author, writing from Jefferson Medical College and Hospital, Philadelphia, discusses the results of histamine gastric analysis carried out on a series of 1,258 subjects as a screening test in the detection of gastric cancer. The choice of this method was prompted by knowledge of the high incidence of achlorhydria and hypochlorhydria in gastric cancer, gastric polyposis, and chronic, particularly atrophic, gastritis. The procedure used was to inject 0·55 mg. of histamine hydrochloride intramuscularly every 20 minutes for 3 doses or until the free acid level, which was determined by titration with Töpfer's reagent, rose to 30 clinical units [30 ml. N/10 hydrochloric acid per 100 ml.] or more; if it was absent, the *p*H was determined with a Beckmann *p*H meter using a glass electrode. When free acid was absent or its level below 30 units after the third dose of histamine further investigations were performed, including radio-

logical examination, gastroscopy, biopsy, and cytological study by the Papanicolaou technique using the Ayer brush.

Of the 1,258 subjects investigated, 487 were male and 771 female, 505 being asymptomatic and 753 symptomatic. Achlorhydria was found in less than 15% of those aged 60 or under, and in more than 20% of those over 60. One asymptomatic patient and 18 with symptoms were found to have cancer of the stomach, an incidence of 17·5 per thousand. Of those with symptoms, the titre of free acid was above 30 clinical units in 4 cases. Other lesions discovered were hiatus hernia (21), gastric polyp (6), gastric ulcer (10), and duodenal ulcer (14). As already noted by other workers, the authors found that most of the 36 patients with atrophic gastritis had achlorhydria, although in a significant number (12), despite the demonstration of atrophy by gastroscopic biopsy, free acid was present. The atrophic changes involved the body of the stomach predominantly. Polyposis was also associated with achlorhydria in all the 6 patients in whom it was diagnosed, while all but one of the 10 with gastric ulcer and all 14 with duodenal ulcer had free acid in the stomach.

In view of the frequent association between atrophic gastritis and gastric cancer a careful follow-up is indicated in cases of the former disease. Although the author found no gastroscopic change in his achlorhydric patients with atrophic gastritis during an observation period of 12 to 18 months, he considers that this should be prolonged to at least 5 years. He does not regard histamine gastric analysis as the ideal screening test for gastric cancer, but owing to its simplicity, which permits its use in the practising physician's surgery, it has much to recommend it as part of a cancer detection programme. The need for intubation is a disadvantage which it may be possible to overcome by the use of quininium resin. *P. I. Reed*

96. **The Physiology of the Gastric Antrum. Experimental Studies on Isolated Antrum Pouches in Dogs**
E. R. WOODWARD, E. S. LYON, J. LANDOR, and L. R. DRAGSTEDT. *Gastroenterology* [*Gastroenterology*] **27**, 766–785, Dec., 1954. 4 figs., 17 refs.

In this paper from the University of Chicago a series of experiments on dogs is described which was designed to demonstrate the influence of the gastric antrum on the secretion of gastric juice by the rest of the stomach. In each animal the antrum was isolated from the rest of the stomach by the construction of a double mucosal bridge leaving its blood and nerve supply intact. The duodenum was transected and the proximal end brought through a stab wound of the abdominal wall as a fistula, the antrum being also provided with a fistulous opening through a stainless steel cannula. In addition, each animal was prepared in one of the following ways: (1) by construction of a denervated Heidenhain pouch and gastro-jejunostomy; (2) by transection of the oesophagus at the gastro-oesophageal junction with closure of the gastric opening, construction of a gastric fistula through a stainless steel cannula, and end-to-side anastomosis between the proximal part of the oesophagus and the first loop of the jejunum; or (3) by construction of a gastric fistula as in (2) and Roux-en-Y anastomosis of the body of the stomach with the jejunum. In animals prepared by the first two methods the fasting gastric secretion contained no free acid, but irrigation of the antrum with solutions of liver preparations and protein hydrolysate at *p*H 5·6 to 6·3 resulted after 1 to 2½ hours in the secretion of free acid. No such effect was produced by irrigation with normal saline or with more acid solutions.

In animals prepared by the third method spontaneous secretion of acid gastric juice was noted in the fasting state, but this ceased promptly on irrigation of the antral pouch with N/10 hydrochloric and other acids (which did not, however, prevent a normal secretory response to the intravenous injection of insulin). The intestinal phase of gastric secretion, observed in an animal prepared by the first method, was not inhibited by acid irrigation of the antrum, and there was no inhibition of the secretion of acid juice produced by histamine in any of the three preparations. Perfusion of an isolated duodenal loop (excluding the pancreatic duct) with N/10 hydrochloric acid had no inhibitory effect on the secretion of gastric juice from a Heidenhain pouch. Distension of the antrum with a rubber balloon filled with water caused a gastric secretory response after 30 to 60 minutes, in an animal prepared by Method 3, but the effect was not constant in all the animals so tested.

The application of 2% cocaine or 1% atropine solution to the antral mucosa abolished the secretory response to irrigation with liver solution and to mechanical distension and the spontaneous secretion of animals prepared by Method 3. Atropine, but not cocaine, abolished the gastric response to insulin hypoglycaemia both when applied to the antral pouch and when administered parenterally. Neither drug had any effect on the histamine response.

The results of these experiments are held to provide further evidence of the secretion by the antrum of a humoral substance, the " gastrin " of Edkins, the inhibition of its production or release by acid irrigation being regarded as a demonstration of the normal mechanism which terminates the gastric phase of gastric secretion in the intact animal. *H. F. Reichenfeld*

97. **Stenosing Antral Gastritis due to Submucosal Hypertrophy.** (Gastriti antrali stenosanti da ipertrofia sottomucosa)
A. LIMENTANI and F. COSTA. *Archivio italiano delle malatti dell'apparato digerente* [*Arch. ital. Mal. Appar. dig.*] **20**, 323–338, 1954. 15 figs., 27 refs.

The authors describe 3 cases of gastritis limited to the submucosa of the antral and pyloric regions, seen at the General Medical Clinic, University of Milan. The first patient, a man aged 31, had a 9-month history of irregular gastric pain. Radiography revealed a sharply defined, tubular narrowing of the antrum with loss of mucosal pattern, a patent pylorus, and delayed gastric emptying. At operation the affected area showed mucosal erosion, and the submucosa was pale,

oedematous, and three times the normal thickness, with enlarged lymph nodes. Microscopically, the mucosal glands were normal but reduced in number, and were clearly separated from a stroma rich in mononuclear leucocytes, lymphocytes, plasma cells, and eosinophil granulocytes. The submucosa was oedematous and hyperplastic, with an increase in the connective and amorphous interfibrillary substance varying in amount from zone to zone. There were lymphoid foci, especially perivascularly, few plasma cells, and a markedly argentophil rete with precollagenous fibres.

In the second case a woman of 65 had a history of some years' epigastric pain and clinical signs of a dilated stomach, while radiography showed a funnel-shaped antral deformity, narrow, indistensible, and immobile, with loss of mucosal folds. At operation the mucosa was seen to be absent in some areas and the muscle thickened and containing amorphous strands. This process stopped abruptly at the pylorus, although the duodenal mucosa was also atrophic. The third patient, a woman aged 41, had a history of 6 months' epigastric pain, signs of gastric stasis, and radiological evidence of a deformed pyloric canal with loss of mucosal pattern. Operation in this case revealed mucosal oedema, muscular thickening, and enlarged fibro-caseous lymph nodes. There was a fistula running from the antrum to the duodenum. Histologically, the mucosa and submucosa showed induration and thickening with typical tubercles. Similar appearances were present in the serosa and connective tissue, but no tubercle bacilli were found.

It is concluded that such conditions are radiologically indistinguishable from neoplasm or from deformities due to perigastritis or postulcerative stenosis.

W. A. Bourne

98. **The Results of Medical Treatment of Peptic Ulcer**
C. A. FLOOD. *Journal of Chronic Diseases* [*J. chron. Dis.*] **1**, 43–50, Jan., 1955. 11 refs.

The immediate and long-term results of routine medical treatment of cases of gastric and duodenal ulcer at the Presbyterian Hospital, New York, are analysed with particular reference to factors which appear to influence prognosis.

The rate of healing of the ulcer crater, as shown by radiographs, varied considerably. The average healing time of gastric ulcer was approximately 6 to 8 weeks; some lesions disappeared in less than 2 weeks, but in a few patients (who at first declined surgical treatment) the ulcer crater persisted for many months before gastric resection was carried out. The healing time of duodenal ulcer was about the same.

Of 101 patients treated medically for gastric ulcer, all except 2 had a recurrence, and of patients treated for duodenal ulcer 78% [exact number not stated] had a recurrence—some more than one—during the subsequent 5 years of medical treatment. On the average there was a recurrence of peptic ulceration once every 2 years, but in patients whose initial response to hospital treatment was slow recurrence tended to be more frequent (average once every 1·2 years). A dietary regimen did not appear to prevent recurrence of symptoms after initial healing of the lesion. In a series of 372 patients with duodenal ulcer haemorrhage recurred at an average interval of about 6 years after the first occasion; after a second haemorrhage there was recurrence once every 3 years. Gastric carcinoma developed in 5 of the 101 patients with gastric ulcer. *Joseph Parness*

99. **A Comparison of Vagotomy and Gastric Resection for Gastrojejunal Ulceration: a Follow-up Study of 301 Cases**
W. WALTERS, D. P. CHANCE, and J. BERKSON. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **100**, 1–10, Jan., 1955. 13 refs.

In this paper from the Mayo Clinic the authors analyse statistically 301 cases in which vagotomy or gastric resection was performed for gastrojejunal ulceration. In 186 cases ulceration occurred after gastro-enterostomy and in 115 after gastrectomy. Treatment of the ulceration was by vagotomy, alone or combined with additional procedures, in 143 and by gastric resection or re-resection in 158 cases.

The mean interval between an initial gastrectomy and operation for gastrojejunal ulceration was 3·7 years, and that between gastro-enterostomy and the second operation was 11·2 years. The authors draw attention to the high incidence of gastrojejunal ulceration in men (90%) and in both men and women after operation for duodenal ulcer (96%). Haemorrhage was a frequent symptom, but, as the authors point out, this is rarely fatal in such cases as there are generally no large vessels in the vicinity of the gastrojejunal anastomosis. They did not find radiological examination of the stomach to be very reliable in diagnosis, especially in cases of ulceration following gastro-enterostomy.

Of the 301 cases, 242 were followed up for one to 8 years, and the final analysis showed that gastrojejunal ulceration after gastro-enterostomy was best treated by gastrectomy (86% good results), and ulceration after gastrectomy by vagotomy alone (70% good results). [The figures for alternative or combined procedures are too small to permit any positive conclusions to be drawn.] *Guy Blackburn*

100. **Partial Gastrectomy with or without Vagus Resection for Duodenal or Marginal Ulcer**
L. T. PALUMBO, T. T. MAZUR, and B. J. DOYLE. *Surgery* [*Surgery*] **36**, 1043–1050, Dec., 1954. 27 refs.

The results of partial gastrectomy with or without vagus resection in 231 patients with duodenal or marginal ulcer are reported from the Veterans Administration Hospital, Des Moines, Iowa. The average duration of symptoms was 10 years and in 60% of the patients there was a history of one or more episodes of haemorrhage. On 189 of the patients standard partial gastrectomy was performed, 22 being operated upon in emergency for massive haemorrhage; 42 patients were subjected to infradiaphragmatic division of the vagus nerve in addition to gastric resection. In all cases three-quarters of the stomach was removed and an antecolic, short-loop anastomosis carried out.

The patients were observed for periods of 6 months to 7½ years, except for 32 of the gastrectomy group and 5 subjected to the combined operation who were lost to follow-up. Mortality in the two groups was comparable (2·5%) provided emergency operations for haematemesis were excluded. Morbidity in the two groups was different: duodenal leakage occurred twice as often after the combined operation as after partial gastrectomy, and whereas there were few immediate complications after gastrectomy, there were two unpleasant sequelae when vagotomy was also performed—namely, gastric atony in 6 patients and diarrhoea and distension in 2.

Late results were more satisfactory in those who underwent resection only. The post-gastrectomy syndrome was observed in 20% and loss of weight in 40% of patients in both groups. Disturbances of alimentary function were most marked in patients subjected to section of the vagus nerve and accounted for the less satisfactory results in this group. Radiography of the small intestine showed persistent delay in emptying with loss of motility in 11 of the patients after vagotomy. Whereas 35% of the patients in the gastrectomy group secreted free hydrochloric acid during a test meal, none of the patients subjected to vagotomy secreted free acid in response to histamine injection or an insulin test meal. A marginal ulcer developed in only 2 patients in the entire series, in both of whom gastrectomy was performed.

Diarrhoea, an infrequent complication of gastrectomy, persists for some time after vagotomy; the authors therefore prefer the former operation. They consider, however, that in tense patients and those in whom there is a marked response to an insulin test meal vagotomy should be performed as well in order to minimize the risk of recurrent ulceration. *A. G. Parks*

LIVER

101. **Therapy in Experimental Hepatic Failure**
P. C. REYNELL. *British Medical Journal* [*Brit. med. J.*] **1**, 459–460, Feb. 19, 1955. 5 refs.

Acute hepatic failure has been produced in rats by the injection of small quantities of carbon tetrachloride into the mesenteric vein. Vitamin supplements, large doses of liver extract, sodium glutamate, and cortisone all failed to reduce mortality in this type of experimental liver failure.—[Author's summary.]

102. **Amino Acid Metabolism in Infectious Hepatitis**
D. Y. Y. HSIA and S. S. GELLIS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **33**, 1603–1610, Dec., 1954. 30 refs.

Amino-acid metabolism was studied at the Children's Medical Center (Harvard Medical School), Boston, in 18 children with acute infective hepatitis. In 6 cases both the total urinary excretion and the plasma level of alpha amino-acids were above the upper limit of normal (as determined in 16 children without hepatic disease). In another 6 cases the urinary excretion was near the upper limit of normal, and in 3 of these the plasma level was increased. In the remaining 6 children the plasma and urinary amino-acid values were within the normal range. The return of abnormal values to normal levels coincided in all cases with clinical recovery. Two-dimensional paper chromatography showed that there was a generalized amino-aciduria, but that most of the increase involved the essential amino-acids.

The authors attribute the changes in amino-acid metabolism to disturbances in deamination. Whether an additional renal defect exists could not be determined in the present study. *P. C. Reynell*

103. **Unexpected Findings on Puncture Biopsy of the Liver.** (Les surprises de la ponction-biopsie du foie)
E. BENHAMOU, B. FERRAND, and J. C. CHICHE. *Presse médicale* [*Presse méd.*] **62**, 1778–1780, Dec. 25, 1954. 17 figs., bibliography.

Basing their conclusions on experience in carrying out some 500 puncture biopsies of the liver without untoward incident at the Medical Clinic, Algiers, the authors claim that in many conditions in which the liver is enlarged, liver biopsy may provide unexpected evidence on which a firm diagnosis can be based or on which a diagnosis may be rejected. Some of these conditions, excluding obvious hepatic lesions, were chronic malaria, tuberculosis, lepromatous leprosy, malignant reticulosis, amyloidosis, and lipoid nephrosis. *C. L. Oakley*

104. **Pruritus of Liver Disease (Xanthomatous Biliary Cirrhosis)**
J. H. HICKS and J. F. MULLINS. *Archives of Dermatology* [*Arch. Derm. (Chicago)*] **71**, 46–51, Jan., 1955. 12 refs.

Generalized pruritus from liver disease without clinical evidence of jaundice is not so rare a syndrome as the literature suggests, and in this paper from the University of Texas 3 cases of xanthomatous biliary cirrhosis are described. [This condition was at one time termed Hanot's cirrhosis, but is better known, perhaps, as pericholangitic cirrhosis.]

The patients, all females, were admitted to hospital with a complaint of generalized itching. Liver biopsy revealed inspissated bile in the small canaliculi with intrahepatic obstruction in one case and "marked triaditis with evidence of obstruction of the bile system" in another. [The histological findings in the third case are not mentioned.] The blood cholesterol level was high. All 3 patients had some pigmentation and early generalized pruritus and anaemia and, at a later stage, developed jaundice. The condition appeared to be due primarily to an inflammatory reaction in the portal area with fibrosis and blockage of the small bile ducts. Whether the high serum cholesterol level was a primary cause or a result of the liver changes was not determined. It seemed likely, however, that the pruritus was due in part to the high serum cholesterol level and in part to some retention of oestrogens in the blood. Methyltestosterone in a dosage of 30 mg. daily was therefore tried in the treatment of these cases. There was complete relief from irritation within 48 hours, but relapse

occurred when testosterone propionate was substituted for the methyltestosterone. The authors noted, as others have done, that although there was dramatic relief of the pruritus, jaundice developed or an existing jaundice deepened. *Thomas Hunt*

105. **Failure of ACTH and Adrenal Corticoids to Alter the Course of Hepatic Coma in Advanced Portal Cirrhosis**
M. SKLAR and I. I. YOUNG. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 138–141, Feb., 1955. 16 refs.

PANCREAS

106. **The Diagnosis of Carcinoma of the Pancreas**
V. M. LEVEAUX. *British Journal of Cancer* [*Brit. J. Cancer*] **8**, 427–433, Sept., 1954. 4 figs., 28 refs.

The literature on carcinoma of the pancreas is reviewed and the diagnosis is discussed in the light of the clinical, radiological, and laboratory findings in 46 cases at the time of admission to the Graduate Hospital, University of Pennsylvania. The average age of the patients (20 females and 26 males) was 60 years. The head of the pancreas was involved in 31 cases, the body alone in 4, the tail alone in 4, and both body and tail in 6; the site in one case was not clearly identified. Pain was by far the commonest initial symptom (29 cases), loss of weight, jaundice, anorexia, and nausea and vomiting being much less frequent.

Radiological examination (with a barium meal) and the glucose tolerance test were the most helpful diagnostic procedures. The serum lipase concentration was of more value in diagnosis than the serum amylase concentration. No other investigations appeared to be of any help. *Roland N. Jones*

107. **A Correlative Study of the External Pancreatic Secretion, the Plasma Antithrombin Titer, the Blood Amylase Concentration, and the Serum Mucoprotein Level in Patients with and without Pancreatic Disease**
D. A. DREILING, E. M. GREENSPAN, and M. SANDERS. *Gastroenterology* [*Gastroenterology*] **27**, 755–765, Dec., 1954. 1 fig., 23 refs.

In view of a report by Innerfield *et al.* (*Amer. J. Med.*, 1952, **12**, 24; *Abstracts of World Medicine*, 1952, **12**, 106) that antithrombin was present in increased quantities in the plasma of patients with acute pancreatitis and other diseases associated with sudden changes in pancreatic function, the authors carried out a controlled investigation of the plasma antithrombin titre in 30 patients with and 49 without evidence of pancreatic disease at the Mount Sinai Hospital, New York. Antithrombin was estimated by Innerfield's technique (*loc. cit.*) in which an elevated titre is defined as " one in which the clotting time of the unknown sample at the 5-minute incubation period is at least 100% greater than the normal control ". The same samples of blood were used for blood amylase and serum mucoprotein determinations, while pancreatic secretory function was studied by means of a secretin test devised by one of the authors in which, after duodenal intubation of the fasting subject, 1·0 unit of secretin per kg. body weight is administered intravenously and the duodenal fluid collected for 80 minutes, its volume, maximum bicarbonate concentration, and total amylase content being determined. The 30 patients suffering from pancreatic disorders included 11 cases of acute and 12 of chronic pancreatitis and 7 of pancreatic carcinoma. The 49 with no pancreatic disease included 6 patients with diabetes mellitus, 6 with sprue syndrome and one with steatorrhoea, 11 with post-cholecystectomy syndrome, and 4 with cholecystitis.

With the exception of one case of acute pancreatitis, the secretin test gave abnormal values in every case of pancreatic disease, whereas the blood amylase and serum mucoprotein content and the plasma antithrombin titres gave little indication of either the presence or absence of pancreatic dysfunction.

In 6 out of the 11 cases of acute pancreatitis, however, the antithrombin titre was increased, and it is considered that its determination may be of diagnostic value in this condition, in which performance of the secretin test may not be feasible. *H. F. Reichenfeld*

SMALL INTESTINE

108. **Primary Tumours of the Small Bowel**
T. A. OGILVIE and H. M. SHAW. *British Medical Journal* [*Brit. med. J.*] **1**, 142–145, Jan. 15, 1955. 6 refs.

The types of primary tumour found in the small intestine, including the duodenum, are briefly described, and 16 cases seen over a 10-year period at the County Hospital, Colchester, are discussed. The lesions included carcinomata (8 cases), sarcomata (5 cases), argentaffin carcinoma (one case), and benign tumours (2 cases), the two last being an adenoma and a leiomyoma respectively. The diagnosis was confirmed on histological examination of material obtained at operation or necropsy. [The authors do not comment on possible differences of opinion among pathologists.]

In the cases of carcinoma symptoms of obstruction occurred late, this being attributed to the fluid nature of the contents of the intestine, and the prognosis was poor because of the rich lymphatic drainage and blood supply to the intestine. The prognosis was also poor in the 5 cases of sarcoma, in 2 of which the tumour was a lymphosarcoma and in 3 a reticulum-celled sarcoma. The argentaffinoma arose in the ileum and had metastasized to the peritoneum, but 3½ years after operation the patient was well and the metastases had not progressed. [No mention is made of the syndrome associated with the secretion of serotonin by malignant argentaffinoma.] The adenoma was situated in the terminal ileum and caused an intussusception, which was reduced and the tumour removed. The leiomyoma occurred in a woman of 50 who presented with melaena; at laparotomy a Meckel's diverticulum was found. [The authors do not state which was the source of the haemorrhage.] *J. E. Richardson*

Cardiovascular System

109. **Effects of Flying on Patients with Cardiovascular Disease**
G. BOURNE. *British Medical Journal* [*Brit. med. J.*] 1, 310–313, Feb. 5, 1955. 3 figs., 2 refs.

Details are given of 30 patients with heart disease who have flown long distances without inconvenience or deleterious effects. The series includes cases of myocardial infarction, angina, hypertension, and severe rheumatic heart disease. In all cases the state of cardiac compensation was good, and adequate pressurization of the aircraft was assured as an essential preliminary to flight.

[These findings confirm the view of most cardiologists that, provided the aircraft is pressurized, flying is as safe as any other method of transport for a patient with heart disease.] *C. W. C. Bain*

110. **Bronchoscopic Approach for Measuring Pressure in Left Auricle, Pulmonary Artery, and Aorta**
P. R. ALLISON and R. J. LINDEN. *Lancet* [*Lancet*] 1, 9–13, Jan. 1, 1955. 10 figs., 8 refs.

The authors have already described their technique of puncture of the left auricle and great vessels through a bronchoscope (*Circulation* (*N.Y.*), 1953, **7**, 669; *Abstracts of World Medicine*, 1954, **15**, 40); in the present paper they report further experience with this procedure, which has now been used in 121 cases without death or serious mishap. The left auricular pressure curves in mitral valve disease with and without auricular fibrillation are analysed, and a simple method for diagnosing mitral regurgitation is described. The authors state that in 59 of 61 cases of mitral valve disease the presence of stenosis or of regurgitation was correctly diagnosed by this method. *S. F. Stephenson*

111. **Treatment of Incapacitated Euthyroid Cardiac Patients with Radioactive Iodine. Summary of Results in Treatment of 1,070 Patients with Angina Pectoris or Congestive Failure**
H. L. BLUMGART, A. S. FREEDBERG, and G. S. KURLAND. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 1–4, Jan. 1, 1955. 2 figs., 11 refs.

Earlier experience of the treatment of incapacitated euthyroid cardiac patients by induction of hypothyroidism with radioactive iodine (^{131}I) has already been reported (*Circulation* (*N.Y.*), 1950, **1**, 1105; *Abstracts of World Medicine*, 1950, **8**, 502). In this paper from Harvard Medical School and Beth Israel Hospital, Boston, the authors analyse the replies to a questionary sent to a number of clinics using ^{131}I in the treatment of euthyroid patients with advanced cardiac disease, the total number of patients being 1,070, including 87 from the authors' clinic.

The dose of ^{131}I varied at the different clinics, a single dose of 50 mc. being given at some. The authors, who point out that too large an initial dose causes radiation thyroiditis and temporary hyperthyroidism, recommend a dose of 10 to 20 mc. each week for 3 weeks, the smaller dose being given to those patients who have attacks of angina at rest or an unduly high uptake of ^{131}I; at intervals of 1 to 2 months additional single doses are given until hypothyroidism is manifest. In patients who have recently been treated with iodine the thyroid gland is de-iodinated by administration of thiourea derivatives.

In 75% of 720 cases of angina pectoris and 60% of 350 cases of congestive cardiac failure there was " worthwhile " symptomatic improvement, the onset of improvement coinciding with the occurrence of hypothyroidism, usually 2 to 6 months after the first treatment. When the patients were clinically myxoedematous desiccated thyroid was given daily, the dosage being adjusted to secure the maximum relief from cardiac symptoms with the minimum of discomfort from myxoedema. Occasionally a further dose of ^{131}I was necessary because of thyroid regeneration. Those patients with congestive failure in whom there was evidence of cardiac reserve benefited most from this treatment. The authors state that the basal metabolic rate should be more than −10% and the patient should be alert, cooperative, and emotionally stable.

It is suggested that the hypercholesterolaemia resulting from the myxoedema does not include further atheromatosis. *D. Goldman*

112. **The Cardiac Output of Normal Subjects Determined by the Dye-injection Method at Rest and during Exercise**
H. J. KOWALSKI, W. H. ABELMANN, W. F. MCNEELY, N. R. FRANK, and L. B. ELLIS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **228**, 622–625, Dec., 1954. 8 refs.

113. **The Mechanism and Significance of the Auricular Sound**
D. WEITZMAN. *British Heart Journal* [*Brit. Heart J.*] **17**, 70–78, Jan., 1955. 6 figs., 21 refs.

The auricular sound, variously referred to as the fourth heart sound, presystolic gallop, or auricular gallop, is a dull, low-pitched sound audible along a line joining the apex to the xiphoid; often it is better felt than heard. It is present in hypertension, cardiac infarction, and certain other conditions, and is frequently associated with left ventricular enlargement. The auricular sound is not audible in the absence of cardiovascular disease or in cases of heart disease in which the radiograph and electrocardiogram are normal. It is often associated with left ventricular enlargement.

From observations at the Institute of Cardiology, London, on 100 patients it is concluded that the auricular sound always indicates abnormality of the ventricle. It occurs 0·12 to 0·17 second after the onset of the P

wave and 0·05 to 0·09 second after the onset of auricular systole, and is a filling sound produced in the ventricle by blood entering during auricular systole.

James W. Brown

114. Myocardial Changes Occurring in Potassium Deficiency

P. M. McALLEN. *British Heart Journal* [*Brit. Heart J.*] **17**, 5–14, Jan., 1955. 10 figs., 38 refs.

The author reports, from the West Middlesex Hospital, London, the myocardial changes observed post mortem in 2 patients in whom prolonged potassium deficiency had been present. The first patient, a man aged 41, had had idiopathic steatorrhoea for over 3 years. The electrocardiogram showed a flat T wave in the standard leads and a slight depression of the S–T segment with an inverted T wave in Leads V_3 and V_5. At this time the serum potassium level was 12·1 mg. per 100 ml. With dietary treatment and the administration of 10 g. of potassium chloride daily these changes disappeared and the patient was discharged. Three years later there was a severe relapse and the patient was readmitted to hospital. The serum potassium level was again very low, and in spite of all treatment he died within a few weeks.

The second patient, a woman of 49, had chronic ulcerative colitis and was under observation for 4 years. During that time she had a series of thrombo-embolic episodes, including one suggestive of cardiac infarction. The electrocardiogram showed a depressed S–T segment and an abnormally low or inverted T wave with a large U wave. The serum potassium level was 11 mg. per 100 ml. and rarely rose above 12 mg. per 100 ml. in spite of large daily doses of potassium. At necropsy widespread myocardial lesions were found in both cases, although the coronary arteries were apparently patent and free from disease. In the second case evidence of focal necrosis of the myocardium was noted. The cardiac lesions are considered to have been the direct result of prolonged potassium deficiency.

H. E. Holling

115. The Effect of Congestive Heart Failure on Blood Volume as Determined by Radiochromium-tagged Red Cells

S. EISENBERG. *Circulation* [*Circulation* (*N.Y.*)] **10**, 902–911, Dec., 1954. 18 refs.

116. Cerebral Hemodynamics in Patients with Heart Failure Associated with Hypertension, and the Response to Treatment

J. H. MOYER, S. I. MILLER, and H. SNYDER. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 121–125, Jan., 1955. 9 refs.

Cerebral blood flow was studied at Baylor University College of Medicine, Houston, Texas, by the nitrous oxide method in 20 hypertensive patients with heart failure and in 6 with valvular heart disease. Although the results were variable, standard treatment of the heart condition had on the average no measurable effect on the (usually normal) cerebral blood flow in the hypertensive patients with cardiac failure. It is considered that when cerebral blood flow is diminished in hypertensive subjects the reduction is due more to arteriosclerosis than to lessened cardiac output. In patients with congestive failure as a result of valvular heart disease, however, the cerebral blood flow was considerably reduced, and in 2 cases treatment for the cardiac lesion was accompanied by a marked improvement in the flow of blood through the brain.

J. McMichael

DIAGNOSTIC METHODS

117. Left Ventricular Hypertrophy. A Study of the Accuracy of Current Electrocardiographic Criteria when Compared with Autopsy Findings in One Hundred Cases

R. C. SCOTT, V. J. SEIWERT, D. L. SIMON, and J. McGUIRE. *Circulation* [*Circulation* (*N.Y.*)] **11**, 89–96, Jan., 1955. 22 refs.

The authors detail the criteria adopted by various [American] authorities for the electrocardiographic diagnosis of left ventricular hypertrophy. These include: (1) high voltage of QRS; (2) delayed onset of the intrinsicoid deflection or prolonged duration of QRS; (3) abnormalities of the RS–T segment or T wave; and (4) prolongation of Q–T. They were applied by the authors in the analysis of 12-lead electrocardiograms from 100 patients who had been shown at necropsy at the Cincinnati General Hospital to have left ventricular hypertrophy (the requirements being a heart weight of more than the expected normal for the length of the body, left ventricular thickness of 13 mm. or more, and right ventricular thickness of 4 mm. or less). The criteria of Wilson *et al.* (*Amer. Heart J.*, 1944, **27**, 19) and of Sokolow and Lyon (ibid., 1949, **37**, 161) were found to be the most accurate and, when combined, were met by 92 of the 100 electrocardiograms. Of the other 8 electrocardiograms, which were all from patients with minimal left ventricular hypertrophy, 3 satisfied the criteria of Katz and one the criteria of Goldberger.

Digitalis had been given to 33 of the patients, in only 11 (33·3%) of whom was the Q–T interval prolonged. Of the remaining 67, the Q–T interval was prolonged in 38 (56·7%). In addition to shortening the Q–T interval (which is prolonged in left ventricular hypertrophy) digitalis may obscure changes in the RS–T segment and T wave and thus affect the accuracy of a diagnosis based on these changes alone.

K. G. Lowe

118. The Distinctive Electrocardiogram of Coronary Arteriospasm

W. EVANS. *British Heart Journal* [*Brit. Heart J.*] **17**, 15–27, Jan., 1955. 14 figs., 20 refs.

A long-term follow-up study over periods of 2 to 10 or more years designed to test the reliability of the electrocardiogram (ECG) in differentiating the pain of cardiac infarction from similar pain with a non-cardiac cause was carried out at the London Hospital on 1,000 consecutive patients with myocardial infarction. A review of their records revealed that in 20 cases the ECG had been regarded as having returned to normal, but in 15 of these further scrutiny of the "normal"

ECG revealed the presence of minor changes which, in the light of more recent experience, showed this view to have been mistaken. These were minor S–T depressions, minor T-wave changes, and an inverted U wave. Thus in 5 cases only did an abnormal tracing eventually become entirely normal. An additional 370 patients were studied who had had similar pain, considered to be of non-cardiac origin, and in whom the ECG was normal when this diagnosis was made; in 4 of these, however, the ECG subsequently showed abnormalities indicating myocardial damage, later reverting to normal in 3 of the 4.

Altogether, therefore, in 8 patients out of 1,370, abnormalities which were present in the ECG at one stage eventually disappeared completely (although exercise caused a temporary return of abnormality). In all 8 the abnormal tracings had a similar pattern, with T-wave inversion in Lead I and sometimes in Lead II, and also in Leads CR_1 and CR_4 and sometimes in Lead CR_7; Q waves and S–T depression were not seen. None of these 8 patients died.

The pattern of these abnormalities indicated a transitory lesion of the anterior wall of the left ventricle, such as would be caused by disease of the anterior descending branch of the left coronary artery. Temporary improvement of the ECG followed the administration of trinitrin to these patients, and the author suggests that the transitory myocardial lesion was caused by spasm of the left coronary artery. He proposes that the distinctive tracing in this type of case be named the " mutable electrocardiogram ". *J. A. Cosh*

CONGENITAL HEART DISEASE

119. **Congenital Heart Disease among Mental Defectives and an Assessment of Cardiac Survey Methods**
C. R. IRELAND, A. C. WITHAM, and H. T. HARPER. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 117–125, Jan. 27, 1955. 3 figs., 21 refs.

The authors have studied the incidence of heart disease, especially congenital lesions, among the 723 inmates of the Georgia Training School, Augusta, Georgia, an institution for mental defectives. The patients were examined clinically, and in all cases a 4-lead electrocardiogram was recorded, the leads used being 1, aFV, and two V leads in modified positions. Before the final diagnosis was reached, however, a 12-lead electrocardiogram was taken and a fluoroscopic examination was carried out.

Acquired heart disease was found in 32 (4·4%) of the patients and congenital heart disease in 17 (2·4%). When these figures were compared with those obtained in healthy subjects of similar age groups it was found that the incidence of congenital heart disease was at least seven times as high in this series as in the general population; there was also some evidence that the incidence of acquired heart disease was higher among mental defectives. Of 86 mongols in the series, 6 (7%) had congenital heart disease. The diagnoses in the remaining 11 cases of congenital cardiac disease were cranial anomaly (1 case), idiocy (2 cases), imbecility (5 cases), and familial moronism (3 cases). It is emphasized that congenital heart disease was found only in those patients whose mental condition was thought to be the result of intra-uterine malformation.

Discussing the diagnostic methods employed, the authors point out that of the 49 cases of heart disease, mass radiography revealed only 7, the 4-lead electrocardiogram 23, and combined electrocardiogram and radiograph 28. Auscultation was necessary for diagnosis in 14 cases and sphygmomanometry in 7.
J. Warwick Buckler

120. **Redistribution of Systemic Blood Flow in Pulmonary Stenosis**
R. J. SHEPHARD. *British Heart Journal* [*Brit. Heart J.*] **17**, 98–104, Jan., 1955. 2 figs., 16 refs.

Peripheral cyanosis is a common finding in cases of pure pulmonary stenosis even in the resting state, and in a large proportion of cases the resting systemic blood flow, as measured at cardiac catheterization by the direct Fick method, is within normal limits. It is believed that in pulmonary stenosis there may be a selective restriction of the blood flow to those sites where cyanosis is commonly observed, particularly the superficial tissues of the extremities. At Guy's Hospital, London, the discrepancy often observed between the clinical estimate of cyanosis and the calculated systemic blood flow was investigated. The oxygen content of the various mixed venous blood specimens obtained at cardiac catheterization in 26 cases of pure pulmonary stenosis, 12 cases of pulmonary stenosis with a patent foramen ovale, and 16 cases of patent ductus arteriosus was analysed. It was found that in pure pulmonary stenosis the blood flow from the upper half of the body exceeded the normal value of 40% of the cardiac output, and that this represented mainly an increased flow to the head. It is suggested that a favourable oxygen tension is maintained in the medullary centres by this selective redistribution of the available cardiac output, and that this explains the rarity of signs and symptoms of medullary hypoxia during exercise in cases of pulmonary stenosis.
James W. Brown

121. **The Brock Operation for Pulmonary Stenosis. Review of Thirty-nine Cases**
N. A. ANTONIUS, A. D. CRECCA, H. A. MURRAY, A. R. RICHLAND, and P. A. IZZO. *Journal of Pediatrics* [*J. Pediat.*] **46**, 54–66, Jan., 1955. 10 refs.

At St. Michael's Hospital, Newark, New Jersey, pulmonary valvotomy was performed by the method of Brock (*Brit. med. J.*, 1948, **1**, 1121; *Abstracts of World Surgery*, 1948, **4**, 287) in 27 cases of Fallot's tetralogy and 12 of pulmonary stenosis with intact ventricular septum; in 11 of the latter there was coexistent interauricular communication [but the direction of the shunt is not specified]. All 39 patients had some degree of dyspnoea and disability. The physical findings and *x*-ray appearances are briefly described. The electrocardiogram showed right bundle-branch block in 3 of the cases of pulmonary stenosis, in 2 of which there were interauricular communications. Cardiac catheterization

revealed infundibular stenosis in only 2 of 11 cases in which this was found at operation. Right ventricular pressure exceeded 100 mg. Hg systolic in 6 out of 10 patients with pulmonary stenosis. Angiocardiography proved unreliable for estimating the degree of overriding of the aorta and for demonstrating infundibular stenosis.

At operation it was found that the site of stenosis was infundibular in most of the cases of Fallot's tetralogy and valvular in most of the others. The results were good in 23 patients and fair in 4; one patient did well for 6 months and then died from a cerebral abscess, and 2 were unimproved. There were 9 operative deaths, 7 of them in children under 6 years of age with severe lesions and often a long, narrow infundibular stenosis which was difficult to correct surgically. In the other 2 fatal cases, both of Fallot's tetralogy, it was believed that the pulmonary valve had been opened too widely. The authors point out that when the valve is opened too widely there is immediate and total relief of cyanosis and the patient's condition appears good. However, recovery from the anaesthetic is slow; the pulse is rapid and the blood pressure low, probably because much of the left ventricular output goes to the lungs, diminishing the systemic output; a little later pulmonary congestion and oedema follow as the left ventricle fails. In some instances death occurs before consciousness is regained. In the authors' view the pulmonary valve should not be opened to the full diameter of the pulmonary artery, and the patient should still be a little cyanosed at the end of the operation. They prefer Blalock's technique to that of Brock for the relief of infundibular stenosis in children under the age of 6 years. *J. A. Cosh*

122. **Considerations and Physiologic Studies in the Closure of Interauricular Septal Defects**
W. H. MULLER, S. W. SMITH, J. F. DAMMANN, F. H. ADAMS, and M. L. DARSIE. *Surgery* [*Surgery*] **37**, 1–14, Jan., 1955. 3 figs., 29 refs.

After a brief review of the history and development of the various methods of effecting closure of auricular septal defects the authors recount their experience at the University of California Medical Center, Los Angeles, in the operative treatment of 18 such cases, in 15 of which the defect was closed through an "atrial well" as described by Gross *et al.* (*New Engl. J. Med.*, 1952, **247**, 455; *Abstracts of World Medicine*, 1953, **13**, 213), and in 3 by atrio-septopexy (Bailey's method).

In all cases the operation was performed through the 4th right intercostal space, the pericardium being opened anterior to the phrenic nerve and a digital examination of the interauricular defect made through the right atrial appendage. If the size, position, and condition of the defect permitted, atrio-septopexy was performed, but in all but 3 of the cases this was not possible. The appendage was therefore closed and the Gross rubber well sutured to a long incision in the posterior aspect of the auricle. Some 200 to 400 ml. of strained citrated blood was placed in the well, the clamps on the auricular wall released, and after cardiac action and blood pressure had become stabilized intracardiac manipulations were begun. The defect was closed with interrupted silk sutures, the rubber well then removed, and the auricular wound repaired.

Good clinical results were obtained in 14 of the patients, as evidenced by reduction in heart size and relief of dyspnoea, of excessive fatiguability, and of the congestive cardiac failure which had been present in 8 cases. Two adults and one child died; both adults had a high degree of pulmonary hypertension, and the child had been in severe heart failure for about 2 years and was actually in failure at the time of the operation. In the 18th case the defect could not be closed and the patient had also a deformed mitral valve. Complications occurred in only 2 cases, in the form of infective pericarditis, but both patients made a good recovery. The intracardiac pressures and total blood volume, which were determined in a number of the patients pre- and post-operatively, are recorded in tables. *C. A. Jackson*

MYOCARDIAL INFARCTION

123. **Can Ward Rounds be a Danger to Patients with Myocardial Infarction?**
K. A. J. JÄRVINEN. *British Medical Journal* [*Brit. med. J.*] **1**, 318–320, Feb. 5, 1955. 6 refs.

Out of 39 patients with myocardial infarction treated at the First Medical Clinic of the University of Helsinki during the period 1950–3 who died 2 to 6 weeks after the attack, 6 died abruptly during a ward round. Three of the deaths occurred while the Physician-in-Chief, on his weekly round, was at the bedside or dealing with the patient in the next bed, and two just after the patient had been told that he was to be discharged. It is concluded that in certain cases the formal ward round may place a dangerously heavy emotional strain on the patient.

[One can only suggest that, if ward rounds arouse such disagreeable emotions in patients with heart disease as to cause their dissolution, there is something wrong with the ritual of the round or with the personality of the physician.] *C. W. C. Bain*

124. **The Relationship between Sudden Changes in Weather and the Occurrence of Acute Myocardial Infarction**
H. C. TENG and H. E. HEYER. *American Heart Journal* [*Amer. Heart J.*] **49**, 9–20, Jan., 1955. 6 figs., 27 refs.

Working at the Southwestern Medical School (University of Texas), Dallas, the authors investigated the relationship between sudden changes in weather and the occurrence of acute myocardial infarction. The town of Dallas is situated in north central Texas about 250 miles inland from the Gulf of Mexico, and at certain seasons is subject to marked changes in temperature (as much as 40° F. (22° C.) in 24 hours) accompanied by considerable changes in barometric pressure, while from June to September the mean daily maximum temperature is 93·2° F. (34° C.).

Between January, 1946, and December, 1951, among 283,931 patients admitted to three Dallas hospitals there

were 1,386 cases of acute myocardial infarction, of which 1,015 occurred in males and 371 in females; 340 (24·5%) of these patients died. The average daily admission rate for cardiac infarction at various seasons was as follows: during stable weather conditions and periods of rain, sleet, or snow, 0·49; at sudden onset of very cold weather, 1·01; at sudden onset of very warm weather, 0·65; and during continued hot weather, 0·7. There was thus a significant increase in the number of cases of cardiac infarction coincident with the sudden onset of cold weather. In the majority of these cases the infarction occurred when the patient was at rest or after meals, in a minority during effort; in about half the cases the infarction occurred while the temperature was falling, in the other half after the temperature had reached its lowest level. Sudden warm weather and prolonged hot weather were also associated with a rise, although slighter, in the incidence of cardiac infarction. But as to what part is played by change in temperature and what by alteration in barometric pressure the authors hazard no guess. *Arthur Willcox*

CHRONIC VALVULAR DISEASE

125. **Mitral Commissurotomy. An Over-all Appraisal of Clinical and Hemodynamic Results**
F. H. Ellis, J. W. Kirklin, R. L. Parker, H. B. Burchell, and E. H. Wood. *Archives of Internal Medicine* [*Arch. intern. Med.*] **94**, 774–784, Nov., 1954. 6 figs., 21 refs.

From the Mayo Clinic the authors report the results of commissurotomy, in which surgical incision was employed in addition to finger fracture, in 131 cases of mitral stenosis. Eleven patients died in hospital, including 8 who were severely incapacitated (Grade IV in the classification of the New York Heart Association); 4 of the deaths were due to cerebral emolism. Of the patients who survived operation, 94 were traced, and re-examination showed that in 59 the results were excellent and in 23 there was significant improvement. In 4 of the latter group symptoms recurred after 6 months; one of these died and necropsy revealed healing of the commissurotomy, which was also believed to have occurred in the remaining 3. A significant factor influencing the results was the preoperative state of the valve, nearly all patients with pliable cusps benefiting whereas almost half of those with immobile valves were unimproved. The operation was a failure in rather more than 40% of patients with preoperative regurgitation, but there was no evidence that surgically-induced regurgitation had any effect. The histological appearances of lung biopsy material were unreliable in predicting the functional response to commissurotomy.

During operation in nearly all the cases there was a fall in pressure in the left atrium to about half the preoperative value, and the mean pressure in the pulmonary artery fell. Cardiac catheterization 3 weeks and again one year later showed that the mean pulmonary arterial pressure was still lower than it was before operation. The pulmonary arteriolar resistance was not affected at the time of operation, but a significant reduction was observed 3 weeks later, which tended to persist. There was a considerable increase in cardiac output in response to exercise in most patients after operation. In the authors' view there is thus physiological evidence of the clinical and symptomatic benefit which follows commissurotomy and which may continue for many months. *M. Meredith Brown*

126. **Pulmonary Haemosiderosis in Mitral Stenosis. Its Relation to Haemodynamic Changes.** (L'hémosidérose pulmonaire dans le rétrécissement mitral. Ses rapports avec les altérations hémodynamiques)
E. Coelho. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 191–204, Jan. 14, 1955. 28 figs., 16 refs.

Writing from the Centre for Cardiological Studies, Lisbon, the author maintains that, contrary to the general belief, irreversible pulmonary haemosiderosis is not a rare condition. Although usually associated with a lesion of the mitral valve, it may occur in children without heart disease and also in cases of congestive heart failure. He distinguishes two forms, a focal type and a diffuse type.

The differential diagnosis of these two types is discussed and the importance of a correct diagnosis emphasized. Diagnosis can be confirmed by bronchial lavage, puncture biopsy of the lung—the method preferred both by patients and by the author—and by examination of a biopsy specimen taken at operation. The puncture-biopsy findings in 40 cases were compared with the pulmonary haemodynamic findings. It was found that the degree of haemosiderosis correlated well with the pulmonary arterial pressure, but a mild haemosiderosis may be found in the presence of normal pressure in the pulmonary circulation. From a study of lung biopsy specimens obtained from 17 cases undergoing valvotomy, the conclusion was reached that there could be a considerable degree of haemosiderosis without any concomitant visible structural damage in the pulmonary vessels [presumably the functional stage of pulmonary hypertension]. Collections of siderophages were also observed, although no apparent reactive changes in the adjoining pulmonary tissues had yet developed. *A. C. Lendrum*

127. **The Determination of "Pulmonary Capillary Pressure Curves" in Mitral Disease.** (Über die Beurteilung von "Lungenkapillardruckkurven" bei Mitralvitien]
W. Overbeck, H. Krook, and G. Biörck. *Zeitschrift für Kreislaufforschung* [*Z. KreislForsch.*] **44**, 22–28, Jan., 1955. 4 figs., 27 refs.

Changes in the pulmonary "capillary" pressure, measured by occluding one pulmonary artery with the tip of an intracardiac catheter, reflect the pressure changes in the left auricle. The authors report an investigation carried out at the Medical Clinic of the University of Lund, Sweden, in which the value of the pulmonary "capillary" pressure curve, recorded electromanometrically, in distinguishing mitral stenosis from mitral incompetence was studied. Curves were obtained on

90 occasions from 79 patients with mitral disease, 11 being investigated both before and after valvotomy. There were 55 patients with pure stenosis (proved at operation in 35 cases) and 24 with combined stenosis and incompetence (proved at operation in 10). A marked presystolic rise in pressure was regarded as evidence of mitral stenosis, a systolic rise as evidence of incompetence.

The results were disappointing, since the majority of the curves were not particularly characteristic. The reasons for this are discussed. The authors imply [though they do not actually state] that tracings of the pulmonary " capillary " pressure are of little value in the differentiation of mitral lesions. *F. Starer*

128. **Radiology of the Lung in Severe Mitral Stenosis**
D. S. SHORT. *British Heart Journal* [*Brit. Heart J.*] **17**, 33–40, Jan., 1955. 9 figs., 9 refs.

The author has reviewed the chest radiographs in 33 selected cases of severe mitral stenosis treated at the London Hospital, in an attempt to correlate the radiological findings with the severity of the lesion. A mitral orifice of 1 cm. or less in length was established at necropsy in 3 cases and at operation in 30. Aortic incompetence was also noted in 5 cases and associated mitral incompetence was found at operation in 13; 12 of the patients had suffered from right heart failure at some period before operation.

In all cases the lungs were considered radiologically abnormal. The left hilum was commonly obscured by the enlarged main pulmonary artery; at the right hilum the pulmonary artery was usually prominent, showing an ill-defined margin against a background of impaired pulmonary translucency. This " clouding " of the lung, present in 30 of the 33 cases, extended generally into the lung field, particularly in the lower part, and was seen to be due to a profusion of shadows cast by smaller vessels. An important sign was the finding in 25 cases of short linear shadows, 5 to 15 mm. long and up to 1 mm. in width, located most commonly in the costophrenic angles. These shadows have been described by Kerley in conditions other than mitral stenosis, and are considered to be caused by thickened interlobular septa lying at right-angles to the pleura. Persistence of these septal shadows after valvotomy suggests that enlargement of the septa is the result of swelling and later fibrosis of the areolar tissue rather than the consequence of lymphatic or venous engorgement. Among other findings were thickening of interlobar pleural fissures in 12 cases and a pleural effusion in one. In only 2 cases was there striking narrowing of the peripheral arterial shadows, as has been described in pulmonary hypertension. Although none of these individual features is peculiar to mitral stenosis the general pattern forms a distinctive picture. The author concludes that a normal lung architecture is inconsistent with a diagnosis of severe mitral stenosis. In discussing radiological technique he points out that to obviate the loss of definition of the hilum and arterial tree caused by pulsation exposures should be as short as possible and should not exceed 0·1 second. *J. A. Cosh*

129. **A New Method of Determining the Degree or Absence of Mitral Obstruction: an Analysis of the Diastolic Part of Indirect Left Atrial Pressure Tracings**
S. G. OWEN and P. WOOD. *British Heart Journal* [*Brit. Heart J.*] **17**, 41–55, Jan., 1955. 15 figs., 28 refs.

A study of the records of indirect left atrial (pulmonary " capillary ") pressure obtained from patients with mitral valve disease suggests that the rate at which pressure falls in the pulmonary venous system when the mitral valve opens is related to the degree of obstruction offered by the valve, the fall of pressure being measured in the descending limb of the *v* wave (the so-called *y* descent). The duration of the *y* descent is variable, being dependent on the length of the diastolic intervals, but the calculated average rate of fall is found to be less variable. The rate of fall, however, also depends on the height of the preceding *v* wave, which must therefore be taken into account. In any patient the least variable indication of the rate of fall of pressure following the opening of the mitral valve was found to be given by the calculated rate of *y* descent in mm. Hg per second divided by the height of the preceding *v* wave in mm. Hg; this quotient is relatively independent of fluctuations in pulmonary vascular pressure and length of diastole. It is suggested that when the left atrial pressure is raised this ratio varies as the pressure–flow relationship across the mitral valve.

In order to confirm this the authors examined the records of 54 patients seen at the Institute of Cardiology and the Brompton Hospital, London, in 30 of whom the degree of stenosis present was known from observation at operation. Comparison of the ratio as calculated and the clinical and surgical findings indicated that if a ratio greater than 1·6 is found it is likely that the mitral stenosis is associated with a significant degree of incompetence. *H. E. Holling*

130. **The Diagnosis of Rheumatic Valvular Disease 1924–1954**
C. BRAMWELL. *Lancet* [*Lancet*] **1**, 213–218, Jan. 29, 1955. 4 figs., bibliography.

131. **The Value of Blood Volume Determinations in the Study of Patients Undergoing Surgery for Rheumatic Heart Disease**
W. LIKOFF, D. BERKOWITZ, S. GEYER, H. STRAUSS, and A. REALE. *American Heart Journal* [*Amer. Heart J.*] **49**, 1–8, Jan., 1955. 1 fig., 8 refs.

In this study of the value of determination of the blood volume of patients undergoing surgery for rheumatic heart disease, carried out at Hahnemann Medical College and Hospital, Philadelphia, the blood volume was determined under fasting basal conditions in 100 such patients and 45 normal controls using radioactive-iodinated human serum albumin (R.I.S.A.) in accordance with the technique described by Storaasli *et al.* (*Surg. Gynec. Obstet.*, 1950, **91**, 458). In analysing the postoperative results morbidity was defined as congestive failure developing within 18 days after operation, and mortality as death due to cardiac causes, but excluding haemorrhage, embolism, and ventricular fibrillation directly

attributable to the operation. The results were as follows (the estimated mean blood volume being given as ml. per kg. body weight). Normal subjects, 75·1; 54 patients without congestive failure, 73·9; 20 patients with failure responding to treatment, 100·3; and 26 with failure not responding to treatment, 86.

Operation on the heart was performed in 59 patients in whom the blood volume was normal or nearly so. After operation 2 died and one developed congestive failure, a morbidity–mortality rate (MM) of 5·6%. On the other hand, of 26 patients with raised blood volume, 4 died after operation and 11 developed congestive failure (MM 57·7%).

The results were also analysed according to the type of valvular lesion present. (1) Of 28 patients with mitral stenosis and normal blood volume, one developed congestive failure (MM 3·5%), and of 8 such patients with raised blood volume, 5 developed congestive failure (MM 62·5%). (2) Of 16 patients with aortic stenosis, none developed complications or died (MM *nil*). (3) Of 13 patients with combined mitral and aortic valvular disease and normal blood volume, 2 died (MM 15·4%), and of 16 such patients with raised blood volume, 2 died and 6 developed congestive failure (MM 56·2%). (4) One patient with mitral incompetence and raised blood volume died after operation.

In 50 (95%) of the 54 patients with chronic rheumatic heart disease who had not been in failure the blood volume was normal. However, in the remaining 4 the blood volume was raised and the postoperative morbidity–mortality was high. The reason for the increase in blood volume is uncertain, but it seems to indicate some change in cardiac physiology which interferes with postoperative progress. The authors consider that determination of the total blood volume serves as a useful guide in the selection of cases for surgery.

Arthur Willcox

132. Aortic Stenosis—Clinical Manifestations and Course of the Disease. Review of One Hundred Proved Cases

J. BERGERON, W. H. ABELMANN, H. VAZQUEZ-MILAN, and L. B. ELLIS. *Archives of Internal Medicine* [*Arch. intern. Med.*] **94**, 911–924, Dec., 1954. 4 figs., 29 refs.

The clinical records are reviewed of 100 cases of aortic stenosis, without other valvular lesions or gross aortic incompetence, which came to necropsy at Boston City Hospital between January, 1943, and November, 1952. The average age of the patients was 69, and the ratio of males to females was 3 : 1. Stenosis was marked in 49 cases, moderate in 32, and mild in 19 In 14 cases there was a history of acute rheumatism, and in 56 there was histological evidence of a rheumatic aetiology of the aortic lesion. The commonest presenting symptoms were dyspnoea (33 cases) and dizziness (25 cases). An aortic systolic murmur was heard in 57 cases, accompanied by a thrill in 25; the loudest murmurs were usually associated with the most marked stenosis. In 29 cases without a systolic murmur at the base an apical systolic murmur, often high-pitched and musical in quality, was heard; in 11 cases there was no murmur. In a number of cases the second aortic sound was not elicited. Severe hypertension was present in some cases—in one the blood pressure was 280/140 mm. Hg—but generally blood pressure varied considerably and was considered to be of limited value in assessing the degree of stenosis. Physical examination showed that the heart was enlarged in 64 cases, while electrocardiography revealed auricular fibrillation in 30. It is of interest that aortic stenosis was diagnosed clinically in only half the cases. Within 2 years of the appearance of congestive cardiac failure, syncope, cardiac pain, or auricular fibrillation half the patients had died, 24 of them suddenly.

G. S. Crockett

133. Aortic Stenosis. A Post-mortem Cinephotographic Study of Valve Action

I. K. R. MCMILLAN. *British Heart Journal* [*Brit. Heart J.*] **17**, 56–62, Jan., 1955. 16 figs., 10 refs.

The author describes a post-mortem cinephotographic study of the aortic valve in action, which he carried out at St. Thomas's Hospital, London, by means of a machine designed to provide pulsatile perfusion of the heart similar to that occurring in life. The apparatus is described. In all, 30 stenosed aortic valves were examined, in 25 of which the effect of a valvotomy post mortem was also observed, while in 6 further cases the valve was examined after surgical valvotomy had been performed during life. Many of these valves remained immobile after valvotomy. Usually it was possible to split only one or two of the commissures, and satisfactory increases in valve area were seldom obtained. On occasions serious damage was done to a mobile cusp and incompetence developed. The presence of calcification, which was noted in no fewer than 27 of the 30 post-mortem specimens, was found to militate seriously against a successful operative result. In the author's view this study demonstrates the urgent need, in the selection of cases for surgical treatment, for some method of direct inspection of the aortic valve.

H. E. Holling

134. Some Hemodynamic Effects of the Hufnagel Operation for Aortic Regurgitation

V. A. MCKUSICK, D. P. HAHN, J. R. BRAYSHAW, and J. O'N. HUMPHRIES. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **95**, 322–337, Dec., 1954. 14 figs., 8 refs.

Hufnagel's operation for the amelioration of the circulatory disturbance in aortic regurgitation involves the insertion of a ball-valve in the descending aorta beyond the mouth of the left subclavian artery. Observations made at the Johns Hopkins University School of Medicine, Baltimore, on models designed to represent conditions before and after the operation suggested that there would be a diminution in volume of the aortic regurgitation, in the diastolic pressure proximal to the ball-valve, and in the intensity of the diastolic murmur (as demonstrated phonocardiographically). The experimental findings (which were confirmed in a patient subjected to the operation) suggested a close relationship between the diastolic pressure and the intensity of the

murmur, but there was no correlation between the degree of change in intensity of the murmur and that in the volume of regurgitation. It was concluded that both the advantages and disadvantages of the operation would be increased by placing the ball-valve closer to the origin of the aorta.

It was difficult to assess the clinical effects of the operation. Giddiness in the upright posture delayed ambulation [as has been reported in other cases] and angina persisted; dyspnoea, which had previously incapacitated the patient, was reduced (though he still restricted his activity) and profuse sweating ceased, but the development of blurring of vision in one eye, due to early optic atrophy and cataract formation, was probably attributable to ischaemia related to the diminished diastolic pressure. Splitting of the sounds produced by the artificial valve was demonstrated by phonocardiography, and its causation is discussed in relation to splitting of the normal second heart sound. The sounds due to opening and closing of the artificial valve were found to fall between the first and second heart sounds. *R. S. Stevens*

135. **Studies in Mitral Stenosis. V. Evaluation of Immediate and Late Results on Fifty Patients, Operated upon since 1950.** [In English]
G. BIÖRCK, O. AXEN, H. B. WULFF, O. LUNDSKOG, H. KROOK, and K. BÜLOW. *Acta medica Scandinavica* [*Acta med. scand.*] **151**, 19–40, Feb. 8, 1955. 4 figs., 21 refs.

DISTURBANCES OF RHYTHM AND CONDUCTION

136. **The Changing Electrocardiogram in Wilson Block**
C. PAPP and K. SHIRLEY SMITH. *Circulation* [*Circulation (N.Y.)*] **11**, 53–68, Jan., 1955. 12 figs., 41 refs.

The authors review 53 consecutive cases, from hospital, consulting, and general practice, of the Wilson (wide-S) type of right bundle-branch block. In 33 cases the patient had probably had myocardial infarction, and in 19 of these there were serial changes in the electrocardiogram (ECG) as follows: (1) normal pattern changing to that of right bundle-branch block; (2) infarction pattern changing to that of transient or persistent right bundle-branch block; (3) pattern of right bundle-branch block changing to infarct pattern; or (4) persistent right bundle-branch block with added infarct pattern showing regression. In 6 patients right bundle-branch block was the sole residual abnormality in the ECG and appeared to be due to a small antero-septal infarct. Right bundle-branch block was associated with one small and 5 large posterior infarcts, 4 of them associated with A-V block.

There was no evidence of myocardial infarction in 20 cases. Nine patients had arteriosclerotic and hypertensive heart disease, 2 had mitral stenosis, one had aortic stenosis, one had an atrial septal defect, 2 had chronic cor pulmonale, 2 had lone auricular fibrillation, and one had paroxysmal auricular flutter. Only 2 out of the 53 patients had right bundle-branch block as the sole cardiac abnormality: one was a youth of 18 and the other a man of 62 in whom the block had first been discovered 19 years before. *K. G. Lowe*

137. **Studies on the Mechanism of Ventricular Activity. XIV. Clinical and Experimental Studies of Accelerated Auriculoventricular Conduction**
J. L. BOURDUAS, L. RAKITA, R. KENNAMER, and M. PRINZMETAL. *Circulation* [*Circulation (N.Y.)*] **11**, 69–88, Jan., 1955. 14 figs., 45 refs.

The authors report from the Cedars of Lebanon Hospital (University of California School of Medicine), Los Angeles, the finding in the electrocardiogram (ECG) of 7 patients of an abnormally short P–R interval of constant or varying duration associated with a normal or abnormal QRS complex. These cases were not examples of the Wolff–Parkinson–White syndrome. Nodal rhythm and partial heart-block occurred in some of the cases, but some showed no evidence of heart disease. The condition was therefore studied experimentally in dogs, in which alteration in the A-V node was produced by the injection of cocaine (20, 5, or 3%), formaldehyde (20%), or acetylstrophanthidin (0·33 to 1·0 ml.; 1 to 3 cat units) into the node. That the point of the needle had entered the A-V node was confirmed by the appearance of transient heart-block or nodal arrhythmias and by post-mortem histological inspection of the site of injection. Of 40 dogs so treated, 11 developed the same alteration in the P–R interval and QRS complex as had been found in the patients, although control injections in other parts of the heart failed to produce such changes. It is assumed that the similarity of the ECG recording in the animals and the patients indicated that in both cases the changes had the same causation.

On these findings the authors base a theory that the A-V node represents the "central nervous system" of the heart and that certain parts of the node supply specified parts of the ventricle. The normal function of the A-V node is then to delay atrio-ventricular conduction, and if this function is disturbed accelerated conduction may take place. If only part of the node is discharged prematurely and the rest discharged later the subsequent QRS complex is wide and aberrant, but remains normal should the whole of the node be discharged prematurely. They consider that the short P–R interval which was observed is unlikely to be due to anomalous anatomical pathways of conduction, which would be expected to function after destruction of the A-V node. That the abnormally short QRS complex is due to interference with the slowing action of the node is suggested by its disappearance when the A-V node is destroyed, either in clinical cases or experimentally in animals.

A suggested clinical classification of A-V nodal abnormalities is presented in the form of a chart, from which it appears that disturbances of the A-V node may give rise to three different conditions: (1) heart-block, (2) accelerated conduction, (3) nodal rhythms and arrhythmias; further, dysfunction of the A-V node may completely change the duration and configuration of the QRS complex. *H. E. Holling*

PULMONARY CIRCULATION

138. **Studies of Pulmonary Hypertension. VI. Pulmonary "Capillary" Pressure in Various Cardiopulmonary Diseases at Rest and under Stress**
P. N. Yu, F. W. Lovejoy, H. A. Joos, R. E. Nye, D. C. Beatty, and J. H. Simpson. *American Heart Journal* [*Amer. Heart J.*] **49**, 31–50, Jan., 1955. 9 figs., 44 refs.

In a study carried out at the University School of Medicine, Rochester, New York, on 150 patients with various cardio-pulmonary diseases pulmonary "capillary" mean pressure (PCm) and pulmonary arterial mean pressure (PAm) were recorded by means of cardiac catheterization at rest and under stress, and from these the pulmonary arterial–pulmonary "capillary" mean pressure gradient (PAm–PCm) was derived. The methods are fully described.

Recordings made at rest showed that the patients fell into four groups. (1) Of 24 patients with raised PAm but normal PCm, that is, precapillary pulmonary hypertension, 16 had chronic pulmonary disease, 5 congenital heart disease, and 3 primary pulmonary hypertension. (2) Of 52 patients in whom both PAm and PCm were raised, that is, with postcapillary pulmonary hypertension, 46 suffered from mitral stenosis and 6 from various other cardiac conditions. (3) Of 69 patients with normal PAm and normal PCm, that is, with no pulmonary hypertension, 33 had congenital heart disease, 12 chronic pulmonary disease, 10 rheumatic heart disease, and 14 miscellaneous cardiac conditions. (4) There were 6 borderline cases in which elevation of PAm or PCm was minimal; these comprised 4 patients with mitral stenosis and 2 with atrial septal defect.

The effect of coughing was recorded in 50 patients; both mean pressures rose, often above 100 mm. Hg. In one patient with chronic pulmonary disease the pulmonary arterial systolic pressure rose to 240 mm. Hg and the pulmonary "capillary" pressure exceeded 120 mm. Hg. The Valsalva manœuvre was studied in 40 patients. In most of them both pressures rose initially to 100 mm. Hg or more, PAm tending to rise more than PCm, and both being then maintained at about twice the normal value. In patients with precapillary pulmonary hypertension exercise caused a rise in PAm but little change in PCm, whereas in patients with postcapillary hypertension both PAm and PCm rose to a high level. Acute hypoxia produced a rise in PAm of more than 5 mm. Hg in 16 patients with mitral stenosis, but none in 2 patients who had undergone valvotomy; the PCm, recorded in 3 cases, rose in 2 and was unaltered in one. In 4 patients with chronic pulmonary disease acute hypoxia caused a rise in PAm, but no change in PCm. In one patient with tricuspid stenosis and in one normal subject the pressures were unchanged.

These results are discussed. Pre- and post-capillary pulmonary hypertension present certain clinical differences, and the authors hold that the determination of PCm is useful in the investigation of pulmonary hypertension. Precapillary pulmonary hypertension occurs in patients with increased pulmonary vascular resistance—for example, in chronic pulmonary disease, in a few cases of cyanotic and late cyanotic congenital heart disease, and in primary pulmonary hypertension; pulmonary oedema is a rare development. Postcapillary pulmonary hypertension occurs in patients with an impaired blood flow through the left ventricle—that is, in mitral disease, left ventricular failure, and constrictive pericarditis; in such cases as these pulmonary oedema is a common complication.

The authors conclude that if PAm is high and PCm normal, then an abnormality of the left side of the heart as a cause of the pulmonary hypertension can be excluded. If, however, both PAm and PCm are raised, then disease of the left side of the heart should be suspected.

Arthur Willcox

PERIPHERAL VASOMOTOR DISTURBANCES

139. **Chilblains**
R. B. Lynn. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **99**, 720–726, Dec., 1954. 8 figs., 5 refs.

Since the term chilblain means "a blotching or ulceration of the skin resulting from (damp) cold" the author prefers it to others which have from time to time been suggested. He discusses two stages in this condition: (1) the acute stage which is completely reversible and is seen in the winter months, disappearing with warm weather; and (2) the chronic stage which is never completely reversible, permanent tissue changes developing and, in some cases, ulceration. More than 75% of patients with acute chilblains are under the age of 20, and females are more often affected than males. The toes, feet, and legs—inadequately and sometimes only partially protected by thin stockings, flimsy footwear, and short skirts—are most frequently involved. When blisters break down, dry dressings should be applied and antibiotics should be given systemically as prophylaxis against secondary infection; excessive heat, vigorous massage, and local applications should be avoided. If exposure to cold is repeated and prolonged, irreversible changes develop in the exposed parts, with permanent discoloration, nodule formation, and finally ulceration of the skin. If ulceration predominates, ulcerative erythema induratum or Bazin's disease is the result.

The author describes 26 cases of chronic chilblains, in all of which there was a history of the acute form of the condition. The ages of the patients, all females, ranged from 16 to 60 years; the average age was 35, but 17 of the patients were under 35. Five of the patients had had poliomyelitis in childhood, and a seasonal incidence in the winter months with regression in the summer months was observed in these and in 17 of the remainder. The author states that there is no specific treatment for chronic chilblains except suitable prophylaxis in any individual who responds abnormally to damp cold. A warm environment, warm clothing, and waterproof footwear are essential. In severe cases with painful ulceration rest in bed with the limbs raised will relieve the symptoms, but excessive warmth will often cause exacerbation of the pain. "Bradosol" (domiphen

bromide) applied locally in a strength of 1 in 1,000 is soothing and non-irritating, and since this is an oily preparation dressings and bed-clothes do not adhere to the ulcer.

The author states that since an essential aetiological factor is chronic arteriolar vasospasm, sympathetic denervation of the involved limbs would seem to be logical. This procedure was carried out on 40 limbs; the results were good, there being no recurrence of ulceration over a follow-up period of 6 years. The subjective improvement was more marked than the objective appearance of the legs suggested. The sensations of coldness, heaviness, and burning and the ulceration were relieved, but the thickened ankles and colour changes were not substantially improved. In conclusion the author states that there is no evidence of a tuberculous aetiology of chilblains. *Leon Gillis*

140. **The Treatment of Peripheral Circulatory Disturbances by Intra-arterial Infusion of Acetylcholine.** (Die Behandlung peripherer Durchblutungsstörungen mit intraarteriellen Dauerinfusionen von Azetylcholin) G. GRABNER, F. KAINDL, and J. PÄRTAN. *Wiener Zeitschrift für innere Medizin und ihre Grenzgebiete* [*Wien. Z. inn. Med.*] **36**, 29–36, Jan., 1955. 4 figs., 3 refs.

The authors suggest that although the intra-arterial injection of acetylcholine is one of the most effective methods of treating peripheral vascular disturbances it is unpopular, partly because the procedure has not been widely practised, and partly because the injection is often painful and, if given rapidly, may cause reflex vasoconstriction. They have therefore adopted the method of slow intravenous infusion, and in this paper from the Second University Medical Clinic, Vienna, they report their experience in giving 707 such infusions to 66 patients, 46 of whom were suffering from arteriosclerosis, 13 from endarteritis obliterans, 3 from Raynaud's disease, and 4 from acute spasm; in 27 cases there were trophic skin changes or gangrene. The majority of the patients, whose ages ranged from 30 to 82 years, had already had some other form of treatment.

An initial dose of 500 mg. of acetylcholine was given, but this was rapidly increased to 1,000 mg. or in some cases to 1,500 mg., the drug being freshly dissolved in 100 ml. of normal saline immediately before infusion. The rate of infusion was adapted to the sensitivity of the patient, and could usually be raised after the first 20 minutes without causing pain; in most cases the infusion was given over 1 to 1½ hours. It is stated that with these quantities and times no acetylcholine passed into the general circulation. In the absence of special apparatus, an intra-arterial infusion set may be improvised from a high-pressure flask and drip chamber, the fluid being forced through with a bellows or with oxygen under pressure from a cylinder. Occasionally the authors found it helpful to aerate the infusion fluid with oxygen, up to 40 to 60 ml. being introduced in 1 to 2 hours. After infusion the puncture site should be compressed for 10 to 15 minutes; the use of anticoagulants is not recommended. In most instances the treatment was given twice a week.

The results were classified into three groups: (1) "good", that is, with disappearance of the trophic changes or of claudication; (2) "improved", but the improvement not definitely attributable to the therapy; (3) no improvement. Of the arteriosclerotic patients, the proportions in the three groups were 70, 24, and 6% respectively, while for the endarteritis cases the figures were 31, 23, and 46% respectively. There were too few cases of other conditions for significant conclusions to be drawn. In general, patients without trophic changes did better than those with such changes. There was no correlation between the result and the patient's age. Fewer infusions were required for the cases of arteriosclerosis than for those of endarteritis and results were obtained more quickly. No untoward effects, such as arterial thrombosis, were observed. Case histories and tables summarizing the results are given and colour photographs of some of the skin lesions before and after treatment are reproduced. *D. Goldman*

HYPERTENSION

141. **Heart-failure from Retention of Salt and Water Caused by Treatment with Pentapyrrolidinium Bitartrate** V. RØNNOV-JESSEN. *Lancet* [*Lancet*] **1**, 122–124, Jan. 15, 1955. 2 figs., 5 refs.

During the past 15 months the author has treated about 100 severely hypertensive patients at Fredericksborg County Central Hospital, Hillerød, Denmark, with pentapyrrolidinium bitartrate ("ansolysen"). Several of the patients had symptoms of heart failure which disappeared during treatment, but 2 patients developed oedema and breathlessness after starting treatment. One was a 52-year-old female who also had mitral stenosis. Her hypertensive headache improved with pentapyrrolidinium, but she developed signs of pulmonary congestion which disappeared when the dose was reduced. The other was a 61-year-old female with hypertensive heart disease. After 5 weeks' treatment with pentapyrrolidinium her weight increased by 11·9 kg. and her haemoglobin level fell from 93 to 73% because of hydraemia. She had severe fatigue and breathlessness on exertion, and there were signs of pulmonary congestion and ascites. The treatment was continued at the same dosage and a mercurial diuretic was given to relieve the fluid retention. Her weight returned to normal and the symptoms of fatigue and breathlessness disappeared. Electrolyte balance studies carried out later on 5 patients in the same series showed that there was reduced excretion of sodium and chloride in the first few days of treatment. This was most pronounced in the case of a 62-year-old female who gave a history of mild breathlessness on exertion and giddiness. Her hypertension responded well to the parenteral administration of pentapyrrolidinium and she felt well during the first few days. However, there was retention of about 30 g. of sodium chloride, hydraemia developed, and her weight increased by 2·5 kg. during 2 weeks' treatment and towards the end of the second week she developed severe orthopnoea and oedema of the ankles.

When a mercurial diuretic was given she had a good diuresis and the breathlessness disappeared.

The author advises that hypertensive patients should be weighed regularly during pentapyrrolidinium treatment and watched for signs of cardiac decompensation, which may require a reduction in the dosage of the drug or treatment with a mercurial diuretic.

K. G. Lowe

142. **The Effect of Hexamethonium upon Cerebral Blood Flow and Metabolism in Patients with Premalignant and Malignant Hypertension**

C. W. CRUMPTON, G. G. ROWE, R. C. CAPPS, J. J. WHITMORE, and Q. R. MURPHY. *Circulation* [*Circulation (N.Y.)*] **11**, 106–109, Jan., 1955. 1 fig., 8 refs.

Measurements of cerebral blood flow and oxygen consumption were made before and 60 minutes after an intramuscular injection of hexamethonium (average dose 1 mg. per kg. body weight) in 13 patients at the University Hospitals, Madison, Wisconsin, with very severe or malignant hypertension. The patients were aged 28 to 48 years, and the blood non-protein nitrogen level was normal in all; 4 had suffered a cerebral vascular accident during the previous year. After the injection of hexamethonium the mean femoral arterial blood pressure fell from 181 to 111 mm. Hg (a decrease of 39%) and the cerebral blood flow fell from 55 to 46 ml. per 100 g. per minute (a decrease of 16%). The cerebral vascular resistance showed a decrease of 29%. There was no significant change in cerebral oxygen consumption despite the fall in cerebral blood flow and a fall in arterial oxygen content, there being a still greater fall in the oxygen content, and a rise in the carbon dioxide content, of internal jugular venous blood.

Comparison of these data with those from studies of the effect on cerebral haemodynamics of differential spinal block reported by Kety *et al.* (*J. clin. Invest.*, 1950, **29**, 402; *Abstracts of World Medicine*, 1950, **8**, 386) suggested to the authors that hexamethonium might have a direct effect on the cerebral blood vessels. They therefore advise that hexamethonium should not be used to lower the mean blood pressure in premalignant or malignant hypertension by more than 30%.

K. G. Lowe

143. **Initial Control of Hypertension with Pentolinium Tartrate**

D. W. ASHBY, J. O'NEILL, and M. C. MACLEAN. *Lancet* [*Lancet*] **1**, 224–228, Jan. 29, 1955. 5 figs., 2 refs.

The method used in the Gateshead Group of Hospitals for stabilizing patients with hypertension on pentolinium tartrate (" ansolysen ") is described. Preliminary investigations when the patient is admitted to hospital include urea clearance tests, intravenous pyelography, and, in relevant cases, tests to exclude the presence of phaeochromocytoma. The authors consider that a control period of several days to determine the resting blood pressure level is not justified on economic grounds. Patients are active during the day and blood pressure is recorded in the erect sitting position every 2 hours from 8 a.m. to midnight, the patient being required to walk twice the length of the ward before blood pressure is taken. For control purposes no treatment is given on the first day. On the following day 1·25 mg. of pentolinium tartrate is injected subcutaneously in the morning and evening, and on subsequent days the dose is gradually increased until the diastolic blood pressure falls to 80 mm. Hg. Thereafter the drug is given by mouth, 40 mg. by this route being regarded as equivalent to 2·5 mg. by subcutaneous injection. This oral dose is increased by 20 mg. daily until the diastolic blood pressure falls to 80 mm. Hg and remains at that level for at least 2 readings on 2 successive days. Some patients receive 2 and some 3 doses during the 24-hour period, the maximum doses being 280 mg. twice daily and 220 mg. thrice daily. Stabilization takes from 4 to 26 days (average 10 days).

Of 72 patients admitted to hospital for treatment with pentolinium tartrate, 26 had to be discharged before treatment was complete and one died from cerebral haemorrhage while in hospital; in the remaining 45 hypertension was satisfactorily controlled before the patient was discharged. Follow-up investigation 3 to 12 months later showed that there was marked relief of symptoms such as breathlessness, headache, and giddiness in about three-quarters of the patients. Of 34 with angina, 6 had complete relief of symptoms and 22 were improved. Of 12 with epistaxis, 11 had no recurrence during the follow-up period. Disturbances of vision due to hypertensive retinopathy did not commonly respond to treatment. Side-effects such as constipation, dryness of the mouth, and blurred vision responded to the usual remedies.

K. G. Lowe

144. **Hemodynamic Effects of 1-Hydrazinophthalazine in Patients with Arterial Hypertension**

G. G. ROWE, J. H. HUSTON, G. M. MAXWELL, A. P. CROSLEY, and C. W. CRUMPTON. *Journal of Clinical Investigation* [*J. clin. Invest.*] **34**, 115–120, Jan., 1955. 16 refs.

The haemodynamic effects of the intravenous injection of 1-hydrazinophthalazine (hydrallazine) were studied at the University of Wisconsin Medical School, Madison, by means of cardiac catheterization in 17 patients with essential hypertension.

In 12 patients injection was accompanied by nasal congestion, palpitation, and facial flushing. In the 5 others the reactions were more severe, consisting in a profound fall in blood pressure, with pallor and nausea or vomiting, and it was impossible to measure the effects until these reactions were over. In the patients with a moderate response the mean arterial pressure fell by an average of 26 mm. Hg, while cardiac output rose by an average of 33%; the pulmonary arterial pressure remained unchanged. In those patients with a more severe reaction the blood pressure fell by 76 mm. Hg, whereas cardiac output remained unchanged, and the pulmonary arterial pressure fell by an average of 5 mm. Hg. One other notable effect of the drug was an increase in the minute volume of respiration. The detailed results for each of the 7 patients are presented in a table.

J. McMichael

Haematology

145. **The Significance of "Dry Tap" Bone Marrow Aspirations**
A. S. WEISBERGER. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 63–68, Jan., 1955. 4 figs., 11 refs.

The author contends that failure to obtain any bone marrow by aspiration from several sites always indicates the existence of some pathological process affecting the marrow, but that such failure should not necessarily be attributed to aplasia of the marrow. He reports the results of the histological examination at Western Reserve University Hospital, Cleveland, Ohio, of specimens of marrow obtained by means of a surgical trephine from 24 patients after aspiration methods had been unsuccessful. (Patients known to have myelofibrosis were excluded.) The diagnosis thus made was of metastatic carcinoma in 6 cases, lymphosarcoma in 4, Hodgkin's disease in 5, sarcoidosis in 2, and histoplasmosis and miliary tuberculosis in one each. In the remaining 5 cases there was only a diffuse fibrosis, but a diagnosis of carcinoma was subsequently made in one of these and of Hodgkin's disease in another, while 2 of the 5 patients subsequently developed monocytic leukaemia, only one remaining quite undiagnosed. All these patients were subsequently found to have extensive involvement of the bone marrow, and in such cases the "dry tap" seems to be due to the resistance of the infiltrating cells to separation or to the accompanying fibrosis. *M. C. G. Israëls*

146. **The Role of the Cerebral Cortex in the Pathogenesis of Transfusion Shock.** (Роль коры головного мозга в патогенезе гемотрарсфузионного шока)
K. V. KUZ'MINA and O. V. LEBEDEVA. *Архив Патологии* [*Arkh. Patol.*] **16**, 61–65, Oct.–Dec., 1954. 20 refs.

In a study carried out at the Lenin Medical Institute, Moscow, the authors have attempted to demonstrate the participation of the cerebral cortex in the pathogenesis of blood-transfusion shock by establishing a conditioned reflex to the introduction of heterogeneous blood. To 2 dogs, on which a total of 84 experiments were carried out, increasing doses of rabbit blood (from 0·15 to 0·6 ml. per kg. body weight) were given intravenously, this being preceded on each occasion by the conditioned stimulus (the ringing of an electric bell). The following observations were recorded: arterial blood pressure, pulse and respiration rate, temperature, general condition of the animal, and examination of the blood for changes in viscosity, coagulability, erythrocyte sedimentation rate, packed cell volume, total protein content, sugar level, haemoglobin value, and erythrocyte and differential leucocyte counts.

After 6 to 14 injections of blood, sham injections were given, accompanied by the same conditioning stimulus. The animals' reactions were found to follow the same pattern as when incompatible blood was injected, but were on the whole somewhat weaker. Even the physical and chemical changes in the blood, although weaker, were of the same nature. Without reinforcement, however, these newly established conditioned reflexes tended to disappear "rather rapidly".

The possibility of using incompatible blood transfusion in shock therapy and in the treatment of peptic ulcer, indolent trophic ulcers, and certain chronic inflammatory conditions is briefly discussed.

A. Swan

ANAEMIA

147. **The Combined Form of Constitutional Haemolytic Jaundice and Pernicious Anaemia.** (Su le forme combinate di ittero emolitico costituzionale e di anemia perniciosa)
G. ERCOLI. *Rassegna di fisiopatologia clinica e terapeutica* [*Rass. Fisiopat. clin. ter.*] **26**, 479–514, July, 1954. 2 figs., bibliography.

The distinction between the constitutional haemolytic anaemias and anaemias of the pernicious type is not always easy to make, and in some cases features characteristic of both types appear to occur together. This is sometimes the case in splenic anaemia of the Strümpell–Bignami type, when the morphological signs of pernicious anaemia occur together with a marked increase in haemolysis and enlargement of the spleen, while hyperchromia, anisocytosis, poikilocytosis, leucopenia, and increased erythrocyte volume may all be observed in other forms of haemolytic jaundice. These mixed forms were described by Chalier as "pernicious anaemic forms of haemolytic jaundice" as far back as 1909. Moreover, megaloblastosis of the bone marrow is no longer generally regarded as being confined to Addisonian pernicious anaemia, since it occurs in other conditions such as leukaemia, secondary anaemia, and severe avitaminosis, and may be produced experimentally by the administration of substances such as aminopterin and ricin. According to Castle, megaloblastosis indicates "a disturbance of the fundamental metabolic process of the cells" which may result from a variety of causes.

The present author reports 8 cases observed at the General Medical Clinic of the University of Pisa, all in members of a single family, in which the features of Addisonian pernicious anaemia were combined with those of a haemolytic anaemia of the Minkowski–Chauffard type. On the basis of the observations made on this group he discusses the clinical significance and the genetics of the haemolytic–pernicious anaemias. He agrees with Cassano and with Cappelli that this type of anaemia cannot be regarded as a separate disease intermediate between pernicious anaemia and consti-

tutional haemolytic anaemia, but that it is due to the combined effect of the causative factors of the two diseases acting together on common dystrophic ground, the form of the anaemia being determined by the degree to which one or other may prevail. This theory assumes the coexistence of two distinct hereditary constitutional faults—the splenomedullary diathesis which is the fundamental cause of haemolytic jaundice, and the defect in the gastric and intestinal mucous membrane which is responsible for pernicious anaemia. *E. Forrai*

148. **Hematological Alterations after Total Gastrectomy. Evolutionary Sequences over a Decade**
M. PAULSON and J. C. HARVEY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 1556–1560, Dec. 25, 1954. 5 figs., 11 refs.

The haematological changes after gastrectomy were studied at varying intervals over a period of 10 years in 27 patients operated on at Johns Hopkins Hospital, Baltimore. The ages of the patients (18 negro and 9 white) ranged from 35 to 65 years. At operation gastric carcinoma was found in 23 cases, lymphosarcoma in 2, benign ulcer in one case, and chronic gastritis in one. Iron-deficiency anaemia was an early feature and was attributed to loss of blood from ulceration at the site of anastomosis. Macrocytosis developed in 19 cases from 6 months to 7 years after the operation; in surviving patients this was invariably followed by anaemia within 1 to 2 years. Examination of the bone marrow in patients who developed macrocytic anaemia [it would appear that there were 9 such patients] revealed megaloblastic erythropoiesis in 5. The interval which elapsed between gastrectomy and the appearance of megaloblastosis ranged from 2½ to 6½ years. In one of these patients atrophy of the jejunal mucosa was found, and it is suggested that this may play a part in depressing intrinsic-factor activity. All the patients with megaloblastic anaemia responded to parenteral administration of cyanocobalamin (vitamin B_{12}); in one case there was a further response to oral administration of folic acid.
L. J. Davis

149. **Metabolic Interrelations between Gastric Intrinsic Hematopoietic Factor and Vitamin B_{12}. II. Further Assays of Vitamin B_{12} in Blood and Urine of Patients with Pernicious Anemia and following Total Gastrectomy by Means of *Escherichia coli* mutant and *Euglena gracilis* Technics**
G. B. J. GLASS, L. C. LILLICK, and L. J. BOYD. *Blood* [*Blood*] **9**, 1127–1140, Dec., 1954. 2 figs., 26 refs.

From the Flower and Fifth Avenue Hospitals (New York Medical College), New York, the authors report the results of further studies of the absorption and utilization of vitamin B_{12} (cyanocobalamin) by patients with pernicious anaemia and after total gastrectomy. After the administration of 100 μg. of vitamin B_{12} intramuscularly to 2 patients who had undergone total gastrectomy the authors found high levels of vitamin B_{12} in the blood as assayed by the *Bacterium* (*Escherichia*) *coli* mutant technique. In 4 patients with pernicious anaemia and one with nutritional macrocytic anaemia a rise in the blood level of vitamin B_{12} to normal was noted after the oral administration of the vitamin together with intrinsic factor from hog's stomach, the more sensitive method of assay with *Euglena gracilis* being used in these cases. The normal level was not, however, maintained throughout oral treatment in spite of both clinical and haematological remissions. The urinary output of vitamin B_{12} was less than 0·5% of the total dose, but the intensity of the haematopoietic response indicates the absorption of much larger amounts of the vitamin from the intestine than this low output would suggest. The authors conclude, therefore, that the vitamin is stored in the tissues. A sharp increase in output noted at the time of the peak of the reticulocyte response in the patients with pernicious anaemia was, they suggest, due to metabolic release of free vitamin B_{12} from its complex binding in the body during hyperactivity of the haematopoietic organs. *Janet Vaughan*

150. **The Nucleic Acid Content of Bone-marrow Cells in Pernicious Anaemia**
H. BREBNER and J. F. WILKINSON. *British Medical Journal* [*Brit. med. J.*] **1**, 379–382, Feb. 12, 1955. 1 fig., 22 refs.

There is as yet no real understanding of the nature of the cellular defect in pernicious anaemia but, the authors suggest, it seems possible that it may be a defect in nucleic acid metabolism. They therefore carried out, at Manchester Royal Infirmary, chemical estimation of the nucleic acid content of bone-marrow cells in sternal marrow samples from 18 patients with classic pernicious anaemia and compared the results with those in 9 samples of marrow showing normoblastic hyperplasia, for greater contrast; in addition 7 samples of normal blood were examined.

The cellular content of ribonucleic acid phosphorus was shown to be higher in pernicious anaemic marrow than in hyperactive normoblastic marrow, indicating that the accumulation of ribonucleic acid in the cell is a specific feature of megaloblastic haematopoiesis. The cells of both these types of hyperactive marrow were found to contain approximately similar amounts of deoxyribonucleic acid phosphorus. Discussing the role of deoxyribonucleic acid in the life of the cell the authors suggest that the high cellular content of deoxyribonucleic acid phosphorus present in the bone marrow in pernicious anaemia may be due, not to some abnormality of mitosis, but to the prevalence in the marrow of cells of proliferative type. *A. W. H. Foxell*

151. **Value of Serum Iron Levels in Assessing Effect of Haematinics in the Macrocytic Anaemias**
C. F. HAWKINS. *British Medical Journal* [*Brit. med. J.*] **1**, 383–385, Feb. 12, 1955. 2 figs., 12 refs.

A study was carried out at the University of Birmingham of the variations in serum iron content, before and after treatment, in the macrocytic anaemias such as pernicious anaemia and those associated with sprue, hepatic disease, and pregnancy. On 100 occasions anaemic patients were given an injection of vitamin B_{12} or folic acid and the serum iron level was estimated at

various intervals. It was found that the effect of haematinics could be reliably assessed by determining the serum iron level before and again 48 hours after an injection, a fall in the serum iron level at 48 hours being probably the earliest sign of a haematological response. The results showed that whatever the serum iron content might be initially, this value tended always to fall to about the same level, namely, 50 to 60 μg. per 100 ml. (normal range 71 to 205 μg. per 100 ml.). Impending iron deficiency was indicated by a fall to a lower level; values below 40 μg. per 100 ml. were suggestive of this, and those below 30 μg. per 100 ml. are considered to be diagnostic of iron deficiency.

It is suggested that this simple test would be of value in assessing the effect of haematinics in macrocytic anaemia, especially in severely ill patients in whom the earliest indication of effective therapy is needed, in cases in which the expected reticulocyte response is small, and also in the treatment of out-patients.

A. W. H. Foxell

152. **Hemolytic Disease of the Newborn due to Anti-A_1**
P. O. HUBINONT, P. LATIERS, and T. MASSART-GUIOT. *Blood* [*Blood*] **10**, 167–175, Feb., 1955. 48 refs.

153. **A Case of Symptomatic Haemolytic Anaemia in Pregnancy**
G. A. CRAIG and R. L. TURNER. *British Medical Journal* [*Brit. med. J.*] **1**, 1003–1005, April 23, 1955. 11 refs.

NEOPLASTIC DISEASES

154. **ACTH and Cortisone in the Treatment of Acute Leukaemia in Children.** (L'ACTH et la cortisone dans le traitement des leucoses aiguës de l'enfant)
R. SACREZ and J. M. LEVY. *Strasbourg médical* [*Strasbourg méd.*] **6**, 1–20, Jan., 1955. Bibliography.

Of 15 cases of acute leukaemia in children seen at the University Children's Clinic, Strasbourg, in the last 2 years and treated with cortisone or ACTH, details are given of the results in only 10, since 5 of the patients were in a hopeless condition on admission. Of these 10, the treatment had no effect or caused deterioration in 2 cases, but resulted in improvement in 4, marked improvement in 2, and complete remission in 2. In 3 of the cases more than one remission occurred.

The following 2 cases are illustrative of the series. In the first, complete clinical and haematological remission occurred in a boy aged 13 whose bone marrow contained 96% of large non-granular leucoblasts. He was first given 50 mg. of cortisone daily, then 100 mg. daily for 6 days, followed by 100 mg. of ACTH daily for 31 days, when the dose had to be reduced to 50 mg. daily for 11 days on account of hypertension and severe dyspnoea. The proportion of leucoblasts in the marrow fell steadily to 44% on the 7th day, 37% on the 25th day, and to 18% on the 35th day. On the 44th day the peripheral blood appeared to be normal, and the marrow contained 7% of unclassifiable cells which did not closely resemble either lymphocytes or leucoblasts. [The duration of the remission in this case is not stated.] In the second case, that of a girl aged 7 who was treated with 75 mg. of ACTH daily for 42 days, there was nearly complete remission for 2 months, when a relapse occurred which was almost uninfluenced by 150 mg. of cortisone daily.

In discussing the choice of treatment the authors state that no rule can be laid down about whether to give cortisone or ACTH. The Thorn test is inapplicable, because eosinophil granulocytes are often absent in acute leukaemia; and the excretion of 17-ketosteroids is very variable, being sometimes reduced and sometimes greatly increased. Remission is most likely to occur in cases treated early, and treatment should not be stopped before complete remission is established; in some cases the maximum effect may not be obtained until about the 49th day. In this series there was no correlation between the length of treatment and the duration of a remission. The authors emphasize that the giving of a maintenance dose is worse than useless since it may cause resistance to further hormone treatment during subsequent relapse.

The type of blast cell present did not appear to influence the response to treatment, but in the present series an initially high leucocyte count appeared to be a sign of resistance to therapy. The longest prolongation of life in these cases was 8 months. It was noted that leucoblastolysis in both the blood and marrow, as well as decrease of mitotic activity, occurred within the first week of treatment, so that leucopenia was common; then in favourable cases normal granulopoiesis and erythropoiesis became established, accompanied by a reticulocytosis of up to 30% or more. Simultaneously the number of platelets usually began to rise.

A. Piney

155. **Oxygenated Nitrogen Mustard in the Treatment of Malignant Haematological [and other] Diseases.** (Le azoipriti ossigenate nella terapia delle emopatie maligne)
G. CONSOLI. *Gazzetta medica italiana* [*Gazz. med. ital.*] **113**, 359–397, Dec., 1954. 23 figs., bibliography.

This paper from the University of Naples describes a trial of di-(2-chloroethyl)-N-oxymethylamine hydrochloride in the treatment of 18 cases of various malignant conditions of the reticuloendothelial system and 3 of epithelial neoplasm. Doses of 50 mg. daily were given, the total dose varying in each case. The full details of all 21 cases are given, and the results obtained with each group of cases discussed very fully. It was found that the drug appeared to be most active against chronic myeloid leukaemia, myeloid reticulosis, Hodgkin's disease, and reticulosarcoma, but not so effective against acute leukaemia. Although there was a marked reduction in the number of cellular elements in the peripheral blood, there was no hypoplasia in the bone marrow. Enlarged lymph nodes rapidly disappeared. Secondary toxic effects were very rare in this series. The action of the drug appears to be slower than that of nitrogen mustard, but the final effect is comparable and its toxicity is considerably less.

R. F. Jennison

Correction: In Abstract 1555 on page 469 of the June issue line 14 for 750 mg. read 250 mg.—[EDITOR.]

Respiratory System

156. **Studies of the Pulmonary Alveolus with the Electron Microscope.** (L'alvéole pulmonaire au microscope électronique)
A. POLICARD, A. COLLET, and L. RALYTE. *Presse médicale* [*Presse méd.*] **62**, 1775–1777, Dec. 25, 1954. 10 figs., 13 refs.

During studies on silicosis carried out at the research laboratories of the Charbonnages de France, Paris–Verneuil, the authors had occasion to examine normal lung tissue of the rat by means of the electron microscope. They report as follows. Electron micrographs of sections of lung 0·1 to 0·2 μ thick and fixed in buffered osmic acid show at magnifications of $\times$6,000 to $\times$18,000 that the alveolar wall consists of two membranes between which are fine reticulin bundles. From the membranes arise capillaries and alveolar cells which project into the alveolar cavities. Where there are no cells or capillaries the two membranes are closely approximated, but in passing round capillaries they separate widely, while the basement membrane of the capillary remains distinct; the space between alveolar and basement membranes contains reticulin bundles.

The alveolar cells, which range from 6 to 15 μ in diameter, are invariably situated between capillaries and show a well-marked nucleus and nucleolus, mitochondria, numerous characteristic vacuoles, and cytoplasmic projections of various sizes; some of these cells were observed passing through the alveolar wall into the interalveolar space. The septal cells, which do not normally project into the alveolar cavities, show a large nucleus and little cytoplasm with numerous membrane-lined splits; mitochondria and cytoplasmic projections are present, but no vacuoles. (All these features are shown in the electron micrographs which are reproduced.)

The authors draw attention to the marked difference in thickness of the alveolar wall as revealed in electron micrographs (0·1 to 0·2 μ) and that seen in conventional preparations (2 μ), and comment on the inadequacy of the demonstration of reticulin fibres in the latter. They believe that electron microscopy, although it raises some new problems, will prove a valuable instrument in the future study of pathological conditions of the lung.

C. L. Oakley

157. **Second Series of Studies of Broncho-emollients. Effect of Succinylcholine.** (Deuxième série de recherches sur les broncho-émollients. Effet de la succinylcholine)
R. BENDA, P. BENDA, E. ORINSTEIN, and P. DELIGNÉ. *Bulletins et mémoires de la Société médicale des hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **70**, 871–878, Oct. 15, 1954. 18 refs.

In this second series of studies on broncho-emollients—the first, carried out in 1947–8, dealt with tubocurarine—the authors, working at the Chest Diseases Centre, Beaujon Hospital, Paris, investigated the effect on the bronchi of intravenous injections of 5 to 30 mg. of succinylcholine given during the course of bronchoscopy carried out under surface analgesia with lignocaine hydrochloride. It was found that even the smallest dose of succinylcholine produced relaxation and loss of muscular tone in the walls of the bronchi, and that this effect allowed the operator to see farther, to visualize the less accessible bronchi more easily, and to obtain a biopsy specimen in cases in which this had previously been impossible under local analgesia alone. In a few cases they supplemented the relaxant with small doses of thiopentone or of chlorpromazine. This seemed to augment the effect of succinylcholine and made the whole procedure even simpler and more comfortable for the patient. They strongly recommend the wider use of this method.

J. Robertson Sinton

158. **An Appreciation of Bronchospirometry as a Method of Investigation Based on 125 Cases**
H. A. FLEMING and L. R. WEST. *Thorax* [*Thorax*] **9**, 273–284, Dec., 1954. 17 figs., 26 refs.

Bronchospirometry with the Carlens catheter was carried out on 113 patients with pulmonary tuberculosis and on 12 patients with other chest diseases at Sully Hospital, Glamorgan. The technique is described in detail and it is emphasized that the procedure is safe and not particularly unpleasant for the patient. A follow-up study showed that apart from slight soreness of the throat and hoarseness in the first few days there were no untoward sequelae, while most patients stated that bronchospirometry was preferable to a visit to the dentist, and to bronchography and bronchoscopy when these had been experienced.

It was confirmed that the right lung accounts for about 55% of total oxygen uptake and ventilation. In most cases changes in the oxygen consumption of a lung were paralleled by changes in the ventilation and vital capacity of that lung. On re-expansion of a lung after pneumothorax and in the bronchiectatic lung, however, oxygen consumption was less than would be expected from their ventilation. A number of cases are described to illustrate the value of this procedure in determining the relative functional capacity of the two lungs and hence in planning treatment. It is also pointed out that assessment of the function of a lung on clinical and radiological grounds is often misleading.

W. A. Briscoe

159. **Spirometric and Bronchospirometric Studies in Five-rib Thoracoplasties**
T. LINDAHL. *Thorax* [*Thorax*] **9**, 285–290, Dec., 1954. 3 figs., 20 refs.

Respiratory function was studied one year or more after thoracoplasty in 23 patients (14 men and 9 women) at Söderby Hospital, Uttran, and Sabbatsberg Hospital, Stockholm. It has already been shown that several factors influence the degree of lung function after thoracoplasty, including the number of ribs resected, pleural

complications, and the degree of scoliosis. In the present investigation these variables were eliminated so far as possible by selecting cases with minimal pleural involvement in which 5-rib thoracoplasty had been performed. It was found that a thoracoplasty on the left side caused more functional defect than one on the right. The maximum breathing capacity was reduced by 2% when the operation was performed on the right and by 8% when it was carried out on the left. Vital capacity was reduced by 13% (right) and 18% (left). Bronchospirometry confirmed these differences between the effects of the operation on the two sides. In cases of right thoracoplasty the oxygen uptake of the operated lung was 46% and in cases of left thoracoplasty it was 30% of the total oxygen uptake.

The author concludes that although the differences are statistically significant they should be verified in a larger series of cases, and that 5-rib thoracoplasty in the presence of minimal pleural involvement has comparatively little effect on lung function. *W. A. Briscoe*

160. **Adenocarcinoma of the Lung.** (Das Adenokarzinom der Lunge)

W. SIEGENTHALER. *Schweizerische medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **85**, 29–34, Jan. 8, 1955. 5 figs., bibliography.

Examination of the necropsy records at the University Pathological Institute, Zürich, confirmed that there has been an increase in the incidence of bronchial carcinoma in recent years. Whereas in 1910 the incidence was 0·17% of all necropsies, it had risen to 1·67% in 1945, and to an annual average of 3·4% for the period 1947–52. In this series bronchial carcinoma has displaced carcinoma of the stomach as the commonest malignant tumour in males. The author believes that this increase is real and not merely the result of improved diagnosis or change in the age of the population. The difficulty of dividing bronchial carcinoma into histological types is recognized. However, a rough classification according to the predominant cell type would be: (1) undifferentiated, (2) squamous-cell carcinoma, and (3) adenocarcinoma. In the present series of 356 bronchial carcinomata, 32·9% were undifferentiated, 57·3% squamous-cell carcinomata, and 9·8% adenocarcinomata.

The author examines 35 cases of adenocarcinoma in detail. He agrees that the majority of these arise from the bronchial mucosa, though a few may originate from mucous glands. No evidence for an origin in the alveolar epithelium was found. In contrast to the other two types the sex incidence in cases of adenocarcinoma was nearly equal, suggesting to the author that this may indicate some fundamental difference between adenocarcinoma and undifferentiated and squamous-cell tumours. The average age of the 35 patients was 59, that is, roughly the same as for the other types. Frequently the primary tumour was small; it gave rise to metastases in 31 (88·6%) of the cases, spread by lymphatics being almost the rule but haematogenous spread also occurred in 27 of the cases. Secondary tumours in the brain were common and the cerebral symptoms frequently predominated. In degree of malignancy these tumours fell between the undifferentiated and the squamous-cell tumours, but clinically they differed in no way from these types.

The author then contrasts bronchial adenocarcinoma with pulmonary adenomatosis [although no cases of the latter condition occurred in his series]. He believes that in this condition the tumours are derived from the alveolar epithelium. Their pathology and clinical course are described and attention is drawn to the similarity between pulmonary adenomatosis and jaagsiekte, a virus disease of sheep. He concludes that there is no relation between pulmonary adenomatosis and bronchial adenocarcinoma. *F. Starer*

161. **Results of Surgical Treatment of Carcinoma of the Lung**

T. HOLMES SELLORS. *British Medical Journal* [*Brit. med. J.*] **1**, 445–448, Feb. 19, 1955. 2 figs., 3 refs.

This paper from the Middlesex, London Chest, and Harefield Hospitals reports in detail a series of cases of carcinoma of the lung operated on by the author between 1940 and 1950 and followed up to the end of 1953. The factors influencing operability are discussed and the opinions are expressed that: (1) straightforward clinical observation is the most satisfactory guide in assessing cardio-respiratory function; (2) a rigid chest, gross emphysema, chronic bronchitis, and persistent bronchospasm are all factors making for a hazardous postoperative course; (3) involvement of the phrenic or recurrent laryngeal nerves, obstruction of the superior vena cava, and involvement of the left auricle causing auricular fibrillation almost always preclude complete excision; (4) oesophageal displacement by enlarged lymph nodes does not always make the case inoperable; and (5) the end-results of operation for squamous-celled carcinomata are better than those for other types, the results in cases of adenocarcinoma and oat-celled carcinoma being uniformly poor.

Despite efforts to achieve an earlier diagnosis, the average delay between early symptoms and operation is still 6 months in the author's cases. The lung and nodes are removed together in the procedure which he adopts, the vessels being divided within the pericardium. The bronchus is divided as close to the carina as possible and closed with interrupted non-absorbable sutures. The case which he would select for lobectomy is that with a small central tumour and without gross lymph-node involvement.

A resection was possible in 446 cases out of the 689 cases explored (pneumonectomy in 364 and lobectomy in 82), and in these cases the operative mortality (death within 4 months of operation) was 18%. A further 29% of patients died between 4 and 12 months after the operation from an early local recurrence or a distant metastasis, often in the brain or an adrenal gland. In all, 47·5% of patients who underwent resection failed to survive for more than a year, and a further 16% died within 2 years. A follow-up of patients treated before 1948 gave a survival rate of 34% at 2 years, 30% at 3 years, 23·5% at 4 years, and 21% at 5 years.

R. L. Hurt

Urogenital System

162. Epidemic Nephritis in a School Population. The Relation of Hematuria to Group A Streptococci
A. C. SIEGEL, C. H. RAMMELKAMP, and H. I. GRIFFEATH. *Pediatrics* [*Pediatrics*] **15**, 33–44, Jan., 1955. 1 fig., 10 refs.

After the development of acute glomerular nephritis in a 5-year-old boy and his 2-year-old sister, both of whom attended the same kindergarten and both of whom had previously suffered from a mild sore throat, throat swabs were taken of the whole school population and of several control groups in the same and other schools. In the kindergarten concerned, over one-third of the 163 children harboured β-haemolytic streptococci, most of which belonged to Type 12, which is known to possess nephritigenic properties. A large number of these carriers were found to have transient microscopic haematuria (with an Addis count in some cases of several thousand erythrocytes per c.mm.), and the urine of 7 of these children also contained erythrocyte casts on at least one occasion, though no other signs of renal damage were found. In contrast, only 11 of the 178 children in the control groups were found to be harbouring β-haemolytic streptococci and only one of these strains belonged to Type 12. *L. H. Worth*

163. The Varied Patterns of Water and Sodium Diuresis during Corticotrophin (ACTH) Therapy of the Nephrotic Syndrome
G. H. HEIDORN, F. R. SCHEMM, and J. A. LAYNE. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 180–187, Feb., 1955. 10 figs., 24 refs.

The purpose of this investigation, carried out at the Montana Deaconess Hospital, Great Falls, Montana, was to obtain further information on the various patterns of water and sodium excretion during and after administration of corticotrophin (ACTH) to patients with the nephrotic syndrome. The effect of ACTH administration on the response to mercurial diuretics was also observed.

For this purpose 7 patients with the syndrome, aged from 4 to 28 years, were investigated, full metabolic studies being performed. ACTH was given intramuscularly in doses of 6 to 12 mg., depending on the patient's age, every 6 hours. Spontaneous diuresis occurred in most cases after discontinuation of ACTH, reaching a maximum in about 24 hours. The change in water diuresis during ACTH administration was also observed, when it was shown that sodium was usually lost in excess of water, although there was considerable individual variation. Mercurial diuretics usually caused a loss of water in excess of sodium when they were given early in the course of ACTH administration. If given later, disproportionately large amounts of sodium were excreted. In one patient who had developed renal tubular resistance to mercurial diuretics, sensitivity was regained during treatment with ACTH. It is suggested that the varied patterns of water and sodium excretion described arise from the correction by ACTH of the abnormally increased amounts of antidiuretic and salt-retaining substances, but that this varies in extent in individual patients and is unpredictable by clinical or laboratory means. The results seem to suggest that the nephrotic syndrome is a composite of numerous defects. The physiopathology of the condition is discussed.
Adrian V. Adams

164. ACTH Treatment of the Nephrotic Syndrome with Reference to Follow-up Findings. (Die ACTH-Therapie des Nephrose-syndroms unter Berücksichtigung der Nachuntersuchungsergebnisse)
W. RUPP, W. SWOBODA, and E. ZWEYMÜLLER. *Helvetica paediatrica acta* [*Helv. paediat. Acta*] **9**, 482–510, 1954. 8 figs., bibliography.

This paper describes the treatment at the Paediatric Clinic, University of Vienna, of 7 children with the nephrotic syndrome and reports the follow-up results in 6 cases to a maximum of 2 years. In all cases detailed laboratory investigations were carried out. ACTH was given in a daily dose of 50 i.u., divided into four 6-hourly doses, for 12 days, the total dosage thus being 600 i.u. The intake of salt was limited to 1 g. daily.

At the start of therapy there was gross oedema in 5 patients and in these the urinary output decreased at first, diuresis beginning only after intervals ranging from 4 days in one case to 12 days in another. Determination of the urinary and blood protein contents showed wide variations in these values. The blood pressure, both diastolic and systolic, rose in all cases and in 2 became so high that cessation of therapy was considered; however, in all cases the blood pressure fell rapidly at the end of treatment. A few complications were noted; urticaria occurred in 2 cases, and treatment had to be suspended in a third case during an attack of bronchopneumonia. No hypokalaemic manifestations were observed. To 2 of the children a second course of ACTH was given. In one case which did not respond a high eosinophil count was thought to be due to a lack of adrenal response and cortisone was therefore tried; this brought about a good clinical and biochemical response, but relapse occurred 4 days after therapy ceased. At the follow-up examination 4 children were found to be so much improved as to be regarded as cured, while in 2 there were temporary remissions, though on the whole they were improved. One child died after developing a true glomerulonephritis. *J. G. Jamieson*

165. Nephrocalcinosis Visible by *X*-ray Associated with Chronic Glomerulonephritis
W. L. ARONS, W. R. CHRISTENSEN, and M. C. SOSMAN. *Annals of Internal Medicine* [*Ann. intern. Med.*] **42**, 260–282, Feb., 1955. 7 figs., 42 refs.

Endocrinology

166. **Endocrine Relations**
D. HUBBLE. *Lancet* [*Lancet*] **1**, 1–5, Jan. 1, 1955. 1 fig., 19 refs.

The author reviews the value of certain diagnostic procedures in distinguishing between endocrine disorders due to primary pituitary failure and those due to the failure of other glands. Two cases of diabetes and thyrotoxicosis of apparently simultaneous onset are described in which the urinary output of 17-ketogenic steroids was increased, and it is suggested that they were true cases of hyperpituitarism. The urinary output of 17-ketosteroids and 17-ketogenic steroids was increased by thyroid therapy in 4 cases of hypothyroidism, and it remains uncertain whether the low level found initially was due to adrenal or pituitary " myxoedema ". In 2 patients with hypopituitarism the impairment of water diuresis in response to a standard load was not removed by cortisone, but slowly improved with thyroid therapy, and it is suggested that thyroid failure was the cause in these cases. Assay of the urinary excretion of 17-ketogenic steroids is considered to be the best test of adrenocortical function.

[This paper cannot readily be abstracted and should be read in the original for its worth to be appreciated.]

B. Nordin

PITUITARY GLAND

167. **Comparative Effects of Intermedin and Corticotropin in Pituitary Insufficiency**
R. M. SALASSA, A. ALBERT, H. L. MASON, M. H. POWER, and R. G. SPRAGUE. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **29**, 619–630, Dec. 8, 1954. 4 figs., 22 refs.

At the Mayo Clinic a 55-year-old man with long-standing severe pituitary insufficiency, which was manifested by exhaustion and marked weakness, offered himself for this study, which was divided into two parts, the first lasting 54 days, the second (7 months later) lasting 84 days. Each part was subdivided into 6-day metabolic periods.

In the first part intermedin, a melanophore hormone of the pituitary gland, was given in increasing doses over 5 successive periods (after 2 control periods). There were no significant effects from a dose of 50 mg. daily for 12 days, but with a dose of 100 mg. daily for the next 12 days, increasing pigmentation of the skin developed and there was a small increase in the output of 17-ketosteroids and adrenocorticosteroids. When the dose was raised to 250 mg. daily for a further 6 days pigmentation increased still further, involving the creases of the palms and the buccal mucosa, and a biopsy specimen from the skin of the neck showed increased deposits of melanin similar to those seen in Addison's disease. Adrenocortical stimulation was more pronounced, with a sharp increase in 17-ketosteroid and corticosteroid excretion and negative nitrogen and potassium balances. These signs of adrenocortical stimulation subsided during 2 final control periods, and the pigmentation gradually faded in the course of the following 8 weeks.

In the second part of the study increasing doses of corticotrophin were given for seven 6-day periods, after two control periods as before. Again there was clear evidence of marked adrenocortical stimulation. During the last 6 days of corticotrophin administration slight pigmentation of the face and knuckles developed, but there was no pigmentation of the buccal mucosa or palmar creases as with intermedin, and a skin biopsy showed no change in melanin content. After adrenocortical stimulation had subsided the patient was given over the next 3 periods 200 mg. of intermedin daily, together with 25 mg. of cortisone, 2 grains (0·13 g.) of dessicated thyroid, and 30 mg. of testosterone propionate. Typical Addisonian pigmentation, confirmed by skin biopsy, again developed; 17-ketosteroid and corticosteroid excretion increased only while the cortisone and testosterone were being given, and there was no metabolic evidence of adrenocortical stimulation. Assay on isolated frog skin in the laboratory showed that the preparation of intermedin used contained 1 unit of corticotrophin per 25 mg.

The authors conclude that these findings support the concept that corticotrophin and intermedin have separate identities. The effect of intermedin is not abolished by administration of doses of cortisone, thyroid, and testosterone which would be considered adequate to maintain a patient with hypopituitarism.

Robert de Mowbray

168. **Puerperal Panhypopituitarism**
I. MACGILLIVRAY and J. F. ADAMS. *Journal of Obstetrics and Gynaecology of the British Empire* [*J. Obstet. Gynaec. Brit. Emp.*] **61**, 738–743, Dec., 1954. 3 figs., 8 refs.

169. **Spontaneous and Induced Water Intoxication in Two Cases of Hypopituitarism**
V. WYNN and O. GARROD. *British Medical Journal* [*Brit. med. J.*] **1**, 505–508, Feb. 26, 1955. 3 figs., 18 refs.

Two cases of Simmonds's disease, seen respectively at St. Mary's Hospital, London, and the Postgraduate Medical School of London, are described. In one case Simmonds's disease followed extirpation of the pituitary gland for acromegaly, and in the other it was associated with postpartum necrosis of the pituitary gland. Both patients had classic signs and symptoms of the disease. A water diuresis test, which was carried out in both cases, resulted in excessive water retention, only 9·0 to 9·5% of the litre of water given being excreted in 3 hours; in addition the test precipitated severe symptoms, in-

cluding great prostration, nausea, vomiting, and mental confusion. Administration of cortisone induced marked diuresis. It is suggested that water retention is not rare in Simmonds's disease and that a water diuresis test should not be carried out when the plasma sodium level is low. *A. C. Crooke*

170. **"Giant-cell Carcinoma" and the other Pituitary Granulomata**

A. G. RICKARDS and P. W. HARVEY. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **23**, 425–440, Oct., 1954. 8 figs., bibliography.

The authors describe 2 cases of giant-cell granuloma affecting the pituitary gland which came to necropsy at hospitals in Salford and Manchester. In one of these cases the pituitary granuloma was a chance finding in a woman of 31 years with ulcerative colitis who died suddenly and unexpectedly and had shown no clinical evidence of hypopituitarism. The anterior pituitary lobe was diffusely infiltrated with giant cells, epithelioid cells, and round cells, though some glandular tissue remained; neither the posterior lobe nor the stalk was involved. The second patient, a woman of 54 years, presented with symptoms of hypothyroidism and visual disturbance leading to almost complete blindness from optic atrophy. Radiography of the skull showed that the pituitary fossa was enlarged and the posterior clinoid processes eroded. The patient died in hypoglycaemic coma. At necropsy a tumour was found which involved the tuber cinereum, the optic chiasma, and both optic nerves. The pituitary gland was almost completely destroyed by dense fibrous tissue within which were occasional giant cells. Adjacent to the gland were many foci of giant-cell granulomatosis, and the posterior lobe could not be identified. Granulomata were also found in the liver.

In a review of previously reported cases of granulomatosis affecting the pituitary gland the authors point out a number of features which differentiate the giant-cell granuloma from other types and which suggest that it is a separate disease entity. Most of the 21 previous cases of giant-cell granuloma occurred in women over the age of 50; evidence of hypopituitarism was lacking in 7 of the 23 cases (including the authors' 2) and in only 2 was diabetes insipidus present, though the anterior lobe was invaded in all cases and the posterior lobe in 4 cases. In contrast, the majority of cases of pituitary involvement in sarcoidosis, syphilis, and tuberculosis occurred under the age of 50 years. The sex incidence was about equal in cases of sarcoidosis and tuberculosis, though in the cases attributable to syphilis women predominated over men in a ratio of about 2 : 1.

In many of the 41 cases of sarcoidosis the lesions involved not only the anterior lobe, but the posterior lobe and infundibulum as well. More than 90% of the patients in this group presented with diabetes insipidus, while symptoms of anterior hypopituitarism occurred in only 4 cases. In most instances the onset of diabetes insipidus was sudden, but developed after the generalized disease had become established. In the 36 cases of pituitary involvement in congenital or acquired syphilis the symptoms were usually those of anterior hypopituitarism, and in only 3 cases did diabetes insipidus occur. In 10 cases, however, the lesions involved not only the anterior lobe, but also the posterior lobe, and in 8 cases the infundibulum was said to have been affected. The lesions were usually gummatous and could be distinguished from giant-cell granulomata by the presence of tissue necrosis and the absence of the optically active particles which are not infrequently present in the latter. Out of 15 cases due to tuberculosis (excluding miliary tuberculosis) the lesions involved the anterior lobe in 12, the posterior lobe in 8, and the stalk in 7. In all cases tuberculosis was also found elsewhere, and the clinical features were extremely variable.

Giant-cell granuloma of the pituitary gland appears, therefore, to be a distinct disease entity. In contrast to other types of granuloma it occurs most commonly after the age of 50 years and predominantly in women. Like syphilis, but unlike sarcoidosis, the symptoms which it causes are predominantly those of anterior hypopituitarism. *Robert de Mowbray*

THYROID GLAND

171. **The value of Radioiodine (I^{131}) in Juvenile Myxoedema Due to Ectopic Thyroid Tissue**

E. M. MCGIRR and J. H. HUTCHISON. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **29**, 561–564, Dec., 1954. 3 figs., 18 refs.

In this paper from Glasgow University the value of tests with radioactive iodine (^{131}I) in juvenile myxoedema associated with ectopic thyroid tissue is discussed and 2 cases are described. In the first case, that of a child of 13 years, the ectopic thyroid tissue had been removed under the impression that it was a thyroglossal cyst. The patient developed myxoedema, and ^{131}I tests indicated the absence of thyroid tissue from the normal site. In the second case, in which there were no obvious signs of myxoedema, similar tests showed that the only thyroid tissue present was situated at the base of the tongue, just above the hyoid bone. There were no local symptoms. In spite of hypothyroidism the plasma in both cases contained appreciable amounts of protein-bound ^{131}I, and it is suggested that this is related to the very rapid turnover of available iodine by the scanty but hyperactive thyroid tissue present in the body. *Winston Turner*

172. **The Menstrual Pattern in Hyperthyroidism and Subsequent Post-therapy Hypothyroidism**

R. C. BENSON and M. E. DAILEY. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **100**, 19–26, Jan., 1955. 6 figs., 7 refs.

The effect of hyperthyroidism and its treatment on the menstrual pattern was studied in 274 patients at the University of California Hospital, San Francisco. Of 221 patients with diffuse toxic goitre, 130 noted a decrease in the amount and duration of the menstrual flow before treatment; an increase was noted by 10, and no change by 81. The menstrual pattern in patients with toxic

recurrent or toxic nodular goitre was somewhat similar. In the majority of cases menstruation became normal after medical or surgical treatment of the hyperthyroidism. Amenorrhoea, which occurred in 20 cases in the series, was always associated with exophthalmos. In 27 cases thyrotoxicosis occurred during pregnancy, but none of these patients had eclampsia.

Hypothyroidism after treatment of thyrotoxicosis was associated with menorrhagia or polymenorrhoea in 18 cases. Menstruation became normal after administration of desiccated thyroid for 1 to 2 months.

Guy Blackburn

173. **The Cerebral Circulation and Metabolism in Hyperthyroidism and Myxedema**

W. SENSENBACH, L. MADISON, S. EISENBERG, and L. OCHS. *Journal of Clinical Investigation* [*J. clin. Invest.*] **33**, 1434–1440, Nov., 1954. 16 refs.

At the Veterans Administration Hospital, Dallas, Texas, of 22 men aged 24 to 64 years suffering from hyperthyroidism, 5 were treated surgically, 14 with radioactive iodine (^{131}I), and 3 with propylthiouracil. In 16 of these (6 having failed to report for follow-up) and in 11 further male patients of similar age suffering from myxoedema (which developed after thyroidectomy in 5 cases, after treatment with ^{131}I in one, was spontaneous in 4, and secondary to hypopituitarism in one) metabolic and cerebral circulatory studies were performed just before treatment and again after it, when the euthyroid state had been restored. The functional state of the thyroid gland was evaluated on the basis of the clinical findings, and on the basal metabolic rate (B.M.R.), uptake of ^{131}I, and serum level of protein-bound iodine. Cerebral blood flow (C.B.F.) was determined by the nitrous oxide method; cerebral oxygen consumption was calculated from the C.B.F. and the cerebral arteriovenous oxygen difference; cerebral glucose consumption from the C.B.F. and the glucose content of cerebral arterial and venous blood; and cerebral vascular resistance from the C.B.F. and the mean arterial blood pressure, the latter being recorded by a damped mercurial manometer from a peripheral artery. These results were analysed statistically by the method of paired observations, the difference between the values being calculated for each subject before and after treatment. The mean of these differences, together with its standard error, was then calculated from the individual differences.

Before treatment hyperthyroidism was found to be accompanied by diminished cerebral vascular resistance and increased cerebral blood flow, and myxoedema by increased cerebral vascular resistance and decreased cerebral blood flow. The cerebral circulation was restored to normal by appropriate treatment. The cerebral consumption of oxygen and glucose was found to be normal in both hyperthyroidism and myxoedema and was unchanged by treatment. *Norval Taylor*

174. **Antithyroid Activity of Some S-Substituted Thiouracils**

H. W. BARRETT and G. L. ELLIOTT. *Science* [*Science*] **21**, 62–63, Jan. 14, 1955. 5 refs.

ADRENAL GLANDS

175. **Cortisone in Exophthalmos**

MEDICAL RESEARCH COUNCIL PANEL. *Lancet* [*Lancet*] **1**, 6–9, Jan. 1, 1955. 5 refs.

For the purposes of an inquiry initiated by the Medical Research Council into the value of cortisone and corticotrophin (ACTH) in the treatment of exophthalmic ophthalmoplegia, 28 patients—10 men and 18 women aged 22 to 79 years—were treated with either cortisone (50 to 200 mg. daily) or ACTH (25 to 100 mg. daily) for periods varying from 6 to 37 days. One patient was classed as "sub-thyroid" and the remainder either as euthyroid or thyrotoxic. A low-sodium diet was given in 4 cases, and all drugs other than the hormones used were discontinued except in the case of one patient who received thyroid extract.

No side-effects were noted. There was no beneficial effect from the treatment in 20 cases; 5 patients showed slight temporary improvement, and 3 responded well. Coexisting thyrotoxicosis was reduced in 8 cases, and the exophthalmos was improved in half of these. It is suggested that the dosage may have been inadequate or insufficiently prolonged in some cases and that the drugs are worthy of further trial in patients with progressive exophthalmos of sudden or recent onset with chemosis.

B. Nordin

176. **Thorn's Test Prolonged over 24 Hours.** (Le test de Thorn prolongé sur 24 heures)

L. DE GENNES, B. MATHIEU DE FOSSEY, H. BRICAIRE, J. GUILLON, and G. DELTOUR. *Annales d'endocrinologie* [*Ann. Endocr.* (*Paris*)] **15**, 653–671, 1954. 7 figs., 8 refs.

In Thorn's original test for estimating the efficiency of the adrenal cortex counts of the eosinophil granulocytes made immediately before and 4 hours after the injection of 25 mg. of ACTH are compared, a fall of less than 50% in the number being taken to indicate adrenal insufficiency. It later became clear, however, that more prolonged adrenal stimulation was needed for reliability, and Thorn himself proposed extension of the period to 48 hours, during which a total of 95 mg. of ACTH would be given.

In this paper from the Hôpital Broussais, Paris, the authors describe in detail their own modification, in which the test is prolonged to 24 hours, 25 mg. of ACTH being injected every 6 hours—the first injection at 8 a.m., the last at 2 a.m.—making a total dose of 100 mg. Eosinophil counts are made immediately before and at 4 hours and 24 hours after the first injection, and 24-hour specimens of urine are collected from the day preceding to the day following the test for estimation of 17-keto- and 11-oxysteroids. The results of the test are classed as follows. (1) Normal (positive): if the mean fall in the 4-hour and 24-hour eosinophil counts exceeds 50% and the daily excretion of 17-ketosteroids is increased by more than 3 mg. (normal 12 to 18 mg. for men, 7 to 10 mg. for women) and that of 11-oxysteroids by more than 20 μg. (normal 30 to 50 μg.). (2) Doubtful: if the mean eosinophil count falls by 30

to 50% and 17-ketosteroid and 11-oxysteroid excretion increase by less than 3 mg. and 20 μg. (3) Pathological (negative): if the mean eosinophil count falls by less than 30% and there is no increase in 17-ketosteroi dor 11-oxysteroid excretion. In normal subjects the results are normal at both 4 and 24 hours, and prolonging the test merely shows that the adrenal response persists under the influence of ACTH. Examination of 52 cases of Addison's disease showed that results were uniformly in accord with the clinical diagnosis; a normal result must be regarded as strong evidence against the diagnosis. In all but 2 of the cases a very low value for the daily 17-ketosteroid excretion was obtained; after administration of ACTH the figure in general remained low, but in 2 cases it became normal, and this part of the test is not therefore considered a reliable criterion of adrenal insufficiency. Determination of 11-oxysteroid excretion gave much more consistent results.

The Thorn test reveals many instances of adrenocortical insufficiency apart from that occurring in Addison's disease. In a study of 24 cases of non-Addisonian asthenia with pigmentation of the skin—a picture suggestive of Addison's disease but differing in its clinical course—prolongation of the test to 24 hours showed its increased diagnostic value. Thus in some of these cases the result was pathological at 4 hours but normal at 24 hours, indicating that the adrenal cortex responded normally to more effective stimulation; in other cases the result of the classic test was normal, but the response at 24 hours pathological, indicating an adrenal cortex incapable of responding to prolonged stimulation. In various other endocrinological conditions, such as myxoedema and pituitary affections, pathological results of the test were recorded in many cases, and similar indication of adrenal insufficiency was found in 2 cases of chronic diarrhoea, while in 6 cases of haemochromatosis the test result was negative in all at 24 hours, although in a few it had been normal at 4 hours.

In conclusion, the authors urge that in order to avoid false pathological results the 24-hour test is essential. Discussing the different elements of the test, they consider the estimation of the daily 17-ketosteroid excretion to be an unreliable guide compared with the eosinophil count and the determination of 11-oxysteroid excretion, and this last, they suggest, should become routine practice. *Kenneth Stone*

177. **Clinical Studies on a New Long-acting Preparation of Adrenocorticotropic Pituitary Hormone Containing Zinc**

C. D. Bonner and F. Homburger. *Bulletin of the New England Medical Center* [*Bull. New Engl. med. Cent.*] **16**, 159–167, Dec., 1954. 5 figs., 14 refs.

When corticotrophin (ACTH) is administered in a gelatin vehicle its action is prolonged. Recently it has been reported that the action of ACTH is not only further prolonged but is also enhanced if the hormone is precipitated with an insoluble zinc salt in aqueous suspension. The present authors, at the Tufts College Medical School, Boston, tried a carboxycellulose purified corticotrophin (Type A) with zinc hydroxide, the potency of which was 12·4 *U.S.P.* units per ml., on 15 patients suffering from various chronic disorders, and compared its effectiveness with that of a gelatin suspension of ACTH.

The potency of the zinc preparation and the duration of its effect were determined by the eosinophil response, the eosinophil count estimated before and 4 hours after intramuscular injection of 40 units of various ACTH preparations being plotted on a graph. For control purposes results were recorded in all cases after administration of 2 ml. of crude liver extract. When gelatin preparations of ACTH were used the eosinophil count generally returned to the pre-injection level within 48 hours; when, however, the zinc preparation was given the eosinophil count was depressed for 56 hours or longer. In 2 patients—one with pemphigus foliaceus and one with atopic dermatitis—whose minimum requirements of ACTH had been well established for many months, the zinc preparation proved to be considerably more potent than the gelatin suspension and its action more prolonged. In the authors' view this enhanced and prolonged action of the zinc preparation permits reduction in the dosage of ACTH and in the number of injections necessary; the preparation is also easier to handle than a gelatin suspension. *Nancy Gough*

178. **Changes in Plasma Levels of 17-Hydroxycorticosteroids during the Intravenous Administration of ACTH. I. A Test of Adrenocortical Capacity in the Human**

K. Eik-Nes, A. A. Sandberg, D. H. Nelson, F. H. Tyler, and L. T. Samuels. *Journal of Clinical Investigation* [*J. clin. Invest.*] **33**, 1502–1508, Nov., 1954. 4 figs., 9 refs.

At the University of Utah College of Medicine, Salt Lake City, the changes in the plasma level of 17-hydroxycorticosteroids were studied in 39 normal subjects and in 6 selected patients with adrenocortical insufficiency during the intravenous administration of ACTH of various potencies in 500 ml. of saline or glucose in water. The subjects were in the fasting state, and none was studied more often than every 10 days. Plasma 17-hydroxycorticosteroid levels were determined by a modification of the method of Nelson and Samuels.

Maximal stimulation of the adrenal cortex was induced by the infusion of 15 to 25 i.u. of ACTH over 6 hours. The administration of 50 i.u. of ACTH did not produce a significantly different response, nor did the infusion of a total of 25 i.u. of ACTH over periods of 2, 4, 6, or 8 hours produce any significant difference in the rate of increase in the plasma 17-hydroxycorticosteroid level. The values increased to a maximum at 6 hours, the standard deviation of the values increasing proportionately to the mean. If the infusion was spread over 8 hours the plasma level at the end of the infusion did not differ significantly from that at 6 hours, and if infusion was continued over many hours the plasma level reached a plateau which was maintained for as long as the infusion was continued. Plasma steroid levels returned to normal within 6 hours of the cessation of the infusion of ACTH.

The responses of the same subject to a standard test of 25 i.u. of ACTH given over 6 hours on different occasions showed considerable variation, which did not seem to be dependent on the control level of plasma 17-hydroxycorticosteroids, or on the animal source of ACTH or its method of preparation. In subjects showing symptoms of Addison's disease there was a decreased response to the test even when the plasma level of 17-hydroxycorticosteroids before infusion of ACTH was within normal limits. *Norval Taylor*

179. **The Effects of 17-Hydroxycorticosterone (Compound F) on Human Eosinophils**
B. HUDSON. *Australian Journal of Experimental Biology and Medical Science* [*Aust. J. exp. Biol. med. Sci.*] **32**, 601–604, Oct., 1954. 14 refs.

Blood was incubated with different concentrations of Compound F for 4 to 6 hours at 38° C. No significant changes were detected in the number of eosinophils in blood rendered incoagulable either by heparin or defibrination. No morphologic changes were detected in the eosinophils. The results of these experiments do not support the hypothesis that eosinolysis is responsible for the phenomenon of hormone induced eosinopenia.—[Author's summary.]

180. **The Influence of Reticuloendothelial Blockade on Hormone-induced Eosinopenia**
B. HUDSON. *Australian Journal of Experimental Biology and Medical Science* [*Aust. J. exp. Biol. med. Sci.*] **32**, 689–693, Oct., 1954. 10 refs.

Reticuloendothelial blockade was induced in guinea-pigs by the use of indian ink and trypan blue. In animals which had been so treated there was no change in (*a*) the ability of cortisone to induce eosinopenia and (*b*) the resting levels of circulating eosinophils before and after reticuloendothelial blockade.—[Author's summary.]

181. **A Colorimetric Reaction for the Estimation of Cortisone, Hydrocortisone, Aldosterone and Related Steroids**
I. CLARK. *Nature* [*Nature (Lond.)*] **175**, 123–124, Jan. 15, 1955. 1 fig., 2 refs.

182. **A Comparative Study of Aldosterone and Other Adrenal Steroids in Adrenalectomized Dogs**
W. W. SWINGLE, R. MAXWELL, M. BEN, C. BAKER, S. J. LEBRIE, and M. EISLER. *Endocrinology* [*Endocrinology*] **55**, 813–821, Dec., 1954. 15 refs.

In a study of the comparative effects of aldosterone and three other adrenocortical steroids, carried out at the University of Princetown, New Jersey, 4 adrenalectomized dogs were tested with each steroid. These 16 animals had been without adrenal glands for 1 to 4 years and had been maintained in good health on a single daily intramuscular injection of 0·5 mg. of deoxycortone acetate in oil and a diet containing 1·47 g. of sodium and 0·94 g. of potassium. Each steroid, in a 10% alcoholic solution, was injected subcutaneously in two divided doses daily, the initial dose being gradually reduced to the minimum maintenance level and this dose continued for at least 10 days except in 2 of the animals treated with aldosterone. The minimum daily maintenance doses were approximately 10 μg. of aldosterone, 125 to 250 μg. of deoxycortone (DOC)—as compared with 300 to 500 μg. daily of DOC in oil—and 5,000 μg. of cortisone or hydrocortisone. A dose of only 0·3 mg. per kg. body weight per day of the 10% alcoholic solution of cortisone or hydrocortisone was necessary for maintenance, compared with a dose of 1·86 mg. per kg. per day in the case of the microcrystalline suspension of these steroids.

The onset of adrenal insufficiency was gradual when the dose was reduced below the minimum maintenance level. The first sign was a fall in arterial blood pressure, unaccompanied in 2 cases by change in the serum levels of sodium and potassium, while a third showed a marked rise in serum potassium level.

The following conclusions were drawn. (1) Aldosterone is 12 to 25 times more potent than deoxycortone. (2) A larger dose of aldosterone is necessary to maintain the arterial blood pressure than to maintain a normal serum electrolyte pattern. (3) Aldosterone is less efficient in preventing the accumulation of excess potassium in the serum than in retaining sodium; of 3 animals in which the serum potassium level exceeded 8·6 mEq. per litre when the sodium level was normal or only slightly reduced, 2 developed severe cardiac symptoms and prostration. (4) The maintenance requirement of aldosterone is 500 times less than that of cortisone or hydrocortisone, but its carbohydrate-regulating activity is of course much weaker, although more powerful than that of deoxycortone. *Robert de Mowbray*

183. **Aldosterone in Urine of Normal Man and of Patients with Oedema**
B. J. AXELRAD, J. E. CATES, B. B. JOHNSON, and J. A. LUETSCHER. *British Medical Journal* [*Brit. med. J.*] **1**, 196–199, Jan. 22, 1955. 19 refs.

The study reported here from Stanford University School of Medicine, San Francisco, was devoted largely to the determination of optimum conditions for the recovery of the aldosterone-like steroids occurring in human urine.

Extracts with chloroform were made at *p*H 6·5 and at *p*H 1·0, and also after 24 hours at *p*H 1·0 and room temperature. Further hydrolysis was also effected with β-glucuronidase. For bioassay, groups of 9 adrenalectomized rats were used, the effect of the extract on the urinary potassium:sodium ratio being compared with that of varying doses of deoxycortone acetate.

Extracts made at *p*H 6·5 showed only insignificant sodium-retaining activity, but when the urine was acidified to *p*H 1·0 before extraction significant activity was found in the urine of a patient with nephrosis and in one with hepatic cirrhosis, but not in that of a healthy subject. No sodium-retaining activity was lost by washing the extract with dilute sodium hydroxide solution. Extracts of urine from healthy adults on normal diet made after standing at room temperature for 24 hours at *p*H 1·0 showed strong sodium-retaining

activity, as also did similar extracts of the urine of normal adults after salt restriction. Extracts made after glucuronidase hydrolysis for 48 hours also showed increased activity, but in general the increase was smaller than after 24 hours at *p*H 1·0. The chromatographic properties of the material studied left no doubt that it was aldosterone. *C. L. Cope*

184. **Non-tuberculous Addison's Disease and its Relationship to "Giant-cell Granuloma" and Multiple Glandular Disease**
A. G. RICKARDS and G. M. BARRETT. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **23**, 403–424, Oct., 1954. 8 figs., bibliography.

The authors describe 3 cases of non-tuberculous Addison's disease which came to necropsy at the Royal Infirmary, Lancaster. All 3 cases occurred in women, aged 56, 51, and 28 years respectively. The youngest was suffering from simple atrophy of the adrenal glands; in the other cases non-caseating granulomata were found, from which no micro-organisms could be recovered. In the first case, although the adrenal glands were chiefly affected, similar lesions were found in the pituitary gland which were, however, not severe enough to produce signs of hypopituitarism. In the second case numerous nodular granulomata were found in the spleen; the adrenal cortex was replaced by dense scar tissue, and the authors suggest that this may have been the result of previous granulomatous involvement. In all 3 cases there were varying degrees of lymphoid infiltration and fibrotic atrophy in the thyroid gland, which was severe enough to produce clinical myxoedema in the first 2 in addition to the picture of Addison's disease.

In a full and critical review of the literature the authors point out that most reported cases of granulomata involving endocrine tissue have presented with signs of hypopituitarism. Although cases have previously been reported in which the adrenal glands have been involved, none of these appears to have presented with Addison's disease or shown signs of myxoedema. Granulomata have been found in other endocrine and non-endocrine structures, notably the testis, spleen, and blood vessels, and it has been suggested that the lesions are a manifestation of a generalized sarcoid reaction. The disease occurs predominantly in middle-aged and elderly women.

As the authors point out, the vast majority of cases of non-tuberculous Addison's disease are due to simple atrophy of the adrenal glands, which in one recent series accounted for as many cases as did tuberculosis. Very rarely other conditions, such as amyloidosis, secondary carcinomatosis, syphilis, mycotic infections, and vascular occlusion, may be responsible, but in most of the reported cases the diagnosis of these conditions has been based on inadequate evidence. Giant-cell granuloma can presumably be added to this list of rare causes, though the diagnosis was established beyond doubt in only one case in this series, and may be responsible also for occasional cases of multiple primary endocrine deficiencies as distinct from those secondary to panhypopituitarism. *Robert de Mowbray*

DIABETES

185. **Insulin Requirements of Children with Diabetes Mellitus Maintained in Good Control**
H. G. KELLY, P. T. RAO, and R. L. JACKSON. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **89**, 31–41, Jan., 1955. 14 figs., 6 refs.

The insulin requirements in relation to growth and certain other factors were studied at the State University of Iowa College of Medicine in 48 children with well-controlled diabetes mellitus. The age at onset of the disease did not influence the insulin requirements materially, but a relationship was observed between insulin needs and growth, a gradual increase in daily dosage corresponding with the period of most rapid growth. In most cases the insulin intake was low for a short period after normal metabolism was restored; it then gradually increased with growth, there being a considerable increase at puberty. The authors point out that when the child reaches adult life the insulin dosage and calorie intake should be adjusted, otherwise obesity will result. *R. S. Illingworth*

186. **Clinical Experience of the Insulin Zinc Suspensions**
J. M. STOWERS and J. D. N. NABARRO. *British Medical Journal* [*Brit. med. J.*] **1**, 68–71, Jan. 8, 1955. 1 fig., 9 refs.

The authors report, from University College Hospital, London, the results of using insulin zinc suspension (I.Z.S.) preparations in the routine management of 240 diabetic patients. This number comprised 35 new cases of diabetes and 205 patients already receiving insulin but in whom either poor diabetic control, or allergy, or the difficulties caused by multiple injections justified the change.

Of the latter group, 81% were satisfactorily controlled with a single injection of the new preparation, and 80% of those with hyperglycaemia, diabetic symptoms, or repeated hypoglycaemia were improved. For most of the patients who had been taking two or three daily doses of soluble insulin little change in the total dosage was needed, but those previously maintained on a single dose of protamine zinc insulin (P.Z.I.) required about 40% more. The authors found that in deciding the initial dose of the new insulin the patient's previous regimen had to be considered. If he had been receiving P.Z.I. alone, they suggest an increase of 20% in the initial dose of insulin zinc suspension; for patients taking globin insulin or P.Z.I. plus soluble insulin an increase of 10%; and for those taking two or three doses of soluble insulin they suggest giving the same total dose as before.

In the majority of cases the standard "insulin lente", which is a mixture of amorphous insulin zinc suspension (I.Z.S.(A)) and crystalline insulin zinc suspension (I.Z.S.(C)) in the proportions of 3 to 7, was satisfactory. In 14% of cases the addition of more I.Z.S.(C) was necessary, and in 2·5% additional I.Z.S.(A) was required. The patients were advised to take their insulin three-quarters to one hour before breakfast in order to prevent the postprandial hyperglycaemia which occurs if the

interval is shorter. As the action of insulin lente is strongest between noon and 6 p.m., the diet was adjusted so that the maximum carbohydrate intake was between these hours. In 10 cases the trial of I.Z.S. had to be abandoned, in 8 of these because of the very large doses of insulin required on transfer. The authors comment that it is not unusual for the diabetes to escape from control on changing to a different type of insulin. The new preparations, however, proved very satisfactory in the stabilization of the 35 new cases of diabetes included in the survey.

Summing up, the authors consider that the insulin zinc suspensions overcome many of the disadvantages of other insulin preparations. The duration of action of I.Z.S. (C) is more than 24 hours, and during the day this can be reinforced with I.Z.S. (A). The actions of mixtures of the two preparations are consistent and predictable, being those of the two components given separately. They conclude that most diabetics are well controlled on the standard mixture (in the proportion of 3 to 7), but a few may require a somewhat different ratio. They close with the warning, however, that in cases where diabetic control has been upset by intercurrent infection the regaining of control is not always easy with these preparations. *John Lister*

187. **Treatment of Diabetes Mellitus with Insulin Zinc Suspensions. A Clinical Study Based on 479 Cases**
K. J. GURLING, J. A. ROBERTSON, H. WHITTAKER, W. OAKLEY, and R. D. LAWRENCE. *British Medical Journal* [*Brit. med. J.*] **1**, 71–74, Jan. 8, 1955. 5 figs., 9 refs.

The authors report their experience at King's College Hospital, London, after one year's trial of insulin zinc suspension (I.Z.S.) in the treatment of 479 diabetic patients, the majority of whom were maintained on the new preparation for over 6 months and all for more than 3 months. At the close of the trial period 433 of the 479 patients were still taking I.Z.S. and in only 32 cases was this form of treatment regarded as a failure. Both subjective and objective factors were considered in assessing the value of I.Z.S. Objectively, the degree of absolute control obtained by I.Z.S. was judged by the degree of night control, as indicated by tests of early morning urine for sugar, by the degree of day control, as judged by the blood sugar level before the midday meal, and by noting any change in the patient's weight exceeding 2 lb. (0·9 kg.) in amount. Subjectively, the value of I.Z.S. was judged by the opinion of the patient concerning his well-being and freedom from hypoglycaemic or diabetic symptoms; it is recognized that this opinion is likely to be biased.

Of 312 adult patients previously receiving other types of insulin, 43% felt better while taking I.Z.S., 55% noticed no change, and 2% felt worse. Night control was good in 67% and unsatisfactory in 33%. Comparison with the previous degree of control showed that 32% were better controlled, 64% equally well controlled, and 4% less well controlled. On changing over from 2 doses of soluble insulin per day or from a mixed dose of soluble and protamine zinc insulin (P.Z.I.) an increase of 10% in total dose was required in 61% of the cases, and in only 28% was no significant alteration required. In patients previously taking a single dose of P.Z.I. a much larger increase was often required. I.Z.S. produced hypoglycaemic reactions in the same way as other insulin preparations; the majority occurred between breakfast and lunch, a smaller proportion being noted between 4 and 6 p.m.

Of the 122 new cases of diabetes in adults included in the series treatment with I.Z.S. was more satisfactory than in the old cases, 102 developing good night control, 98 good day control, and 110 gaining weight. The series also included 45 children, the youngest being 2 years of age. Of the 30 old cases among these children good control was obtained in 12 on changing to I.Z.S., fair control in 17, and in only one was control inadequate. Of the 15 new cases in children good control was obtained in 12, the remaining 3 cases being fairly well controlled.

At the close of the trial 46 of the 479 patients were no longer taking I.Z.S., but only 32 (7%) of these were regarded as cases of failure, for which the most common reason was poor control. The authors consider that the introduction of I.Z.S. should result in an increasing number of diabetics being adequately controlled on one injection of insulin a day. In an addendum to their paper, however, they point out that further experience has shown that there exists a group of patients in whom I.Z.S. fails to control hyperglycaemia and prevent ketosis. These are cases which are relatively insensitive to the long-acting insulin preparations, and cannot successfully be treated for any length of time without the use of soluble insulin. *John Lister*

188. **Triopathy of Diabetes. Sequence of Neuropathy, Retinopathy, and Nephropathy in One Hundred Fifty-five Patients**
H. F. ROOT, W. H. POTE, and H. FREHNER. *Archives of Internal Medicine* [*Arch. intern. Med.*] **94**, 931–941, Dec., 1954. 15 refs.

The term "triopathy of diabetes" is used by the authors for the sequence of complications observed in many cases of long-standing diabetes—namely, neuropathy, retinopathy, and nephropathy. The signs and symptoms of diabetic neuropathy are neuritis, paraesthesiae, nocturnal pain, objective loss of sensation, disturbances of the autonomic nervous system, such as nocturnal diarrhoea, and pseudo-Charcot joints. The authors state that the incidence of neuropathy varies according to the observer's definition—for example, if impaired vibration sense is accepted as diagnostic "probably 95% of patients over 30 years of age with uncontrolled diabetes" would be considered to have neuropathy. The micro-aneurysms of diabetic retinopathy [first described by Stephen McKenzie in 1887] sometimes precede the diabetes; in the later stages of the disease hard, waxy retinal exudates are seen. Diabetic nephropathy begins with albuminuria; later, oedema and hypertension develop, retinal lesions become worse, and finally there is renal failure.

The authors then discuss the incidence of these complications in a series of 2,288 patients with diabetes

admitted to the New England Deaconess Hospital, Boston, in the year ending December, 1953. They were present in 784 of the patients—retinopathy in 265, nephropathy in 147, and neuropathy in 228 patients, while all three complications were present in 71, and retinitis proliferans in the remaining 73. The duration of the diabetes appeared to be causally related to the incidence of complications, since in 88 out of 155 complicated cases which came under the authors' care the disease had been present for 10 to 19 years.

It is pointed out that the new staining techniques for mucopolysaccharides have shown that the staining material present in these capillary aneurysms of the retina is the same as that found in Kimmelstiel–Wilson lesions in the kidneys.

[This is an excellent review of the complications of diabetes.] *I. McLean Baird*

189. **Hypophysectomy in Human Diabetes. Metabolic and Clinical Observations in Diabetics with Malignant Vascular Disease**

L. W. KINSELL, L. LAWRENCE, H. E. BALCH, and R. D. WEYAND. *Diabetes* [*Diabetes*] 3, 358–366, Sept.–Oct., 1954 [received Dec., 1954]. 4 figs., 4 refs.

The cause of the rapid progression of vascular disease in cases of long-standing diabetes, especially in those in which the disease has been present since childhood, remains undetermined. Strict control of the diabetes will reduce this tendency, but it is doubtful whether it can be eliminated altogether by this means alone. The vascular damage associated with Cushing's syndrome and the vascular changes produced in diabetic animals by the administration of corticoids suggest that chronic adrenal hyperfunction may be one of the factors concerned, and if this is so, treatment should be directed towards the reduction of this excessive production of adrenal steroids. In the absence of any hormonal agent whereby this might be achieved, the authors have carried out hypophysectomy in 4 cases of juvenile diabetes with well-established vascular disease at the Samuel Merritt and Highland–Alameda County Hospitals, Oakland, California. The first 2 patients thus treated were aged 31 and 26 years respectively and had both had diabetes since the age of 13. Both had extensive retinal, renal, and cardiac damage. The first died 4 months after operation from cardiac and renal failure, and the second, though free of oedema when he left hospital, died a month later from coronary occlusion. In the third and fourth cases the vascular disease was less advanced, and the patients were still alive 5 and 3 months respectively after the operation, the renal and cardiac condition having improved in each case.

Discussing the principles governing the management of such cases, the authors point out that preoperatively, apart from the control of the diabetes, problems resulting from myocardial and renal insufficiency must be faced, while anaemia and hypoproteinaemia may also be present. After the operation the effects of pituitary insufficiency require treatment in addition; these include hypoadrenocorticism, hypothyroidism, and hypogonadism, while the patient's previous state of insulin resistance is changed to one of insulin hypersensitivity. For 2 days before operation the authors' patients were given intravenous infusions containing glucose, sodium chloride, potassium chloride, insulin, and the vitamin-B complex. Cortisone (50 mg.) was given intramuscularly 12-hourly during this period, and hydrocortisone (100 mg.) was given intravenously to cover the operation itself. Postoperatively the patients were maintained for several days by intravenous infusion. Cortisone was given in doses of 50 mg. 12-hourly intramuscularly for the first 3 days and the dose then reduced as indicated by the urinary output, blood pressure, and blood sugar level. The difficulty of control of electrolyte balance was found to be closely related to the degree of renal damage present, and the greatest danger appeared to be that of cerebral oedema. The judicious use of intravenous infusions of serum albumin, the administration of sodium and potassium so as to maintain the plasma level of the former slighly below and of the latter slightly above normal, and the total avoidance of deoxycortone seemed to be the most important points.

The authors admit that from their small series they can draw no valid conclusions as to the value of hypophysectomy in cases of malignant diabetic vascular disease. They believe, however, that it is a justifiable procedure when the vascular condition is rapidly progressing but the renal reserve is still adequate.

John Lister

190. **Adrenalectomy in Human Diabetes. Effects in Diabetics with Advanced Vascular Disease.**

J. T. WORTHAM and J. W. HEADSTREAM. *Diabetes* [*Diabetes*] 3, 367–374, Sept.–Oct., 1954. 9 figs., 17 refs.

The authors report the results of total adrenalectomy in 7 cases of diabetes with severe degenerative vascular disease. The patients varied in age from 23 to 54 years, and in all but 2 cases the disease had been present for more than 13 years. Nearly all had a history of poor diabetic control and all had evidence of extensive vascular disease as manifested by hypertension, albuminuria, oedema, and retinal change.

After adrenalectomy the patients were maintained with cortisone or hydrocortisone only. In 4 cases there was either arrest of, or improvement in, the retinal changes and in 4 cases there was a slight fall in blood pressure. The degree of albuminuria and oedema was reduced in 3 cases, and in 5 there was a reduction in insulin requirements in spite of the diabetogenic nature of the maintenance therapy. The instability characteristic of diabetes occurring in cases of Addison's disease was not observed.

At the time of the report 4 patients were living and 3 had died. In 2 of the survivors remission of the degenerative process had been sustained for periods of 10 and 14 months respectively, with improvement in the retinal condition, a decrease in proteinuria and oedema, and a return of the blood pressure to normal levels. Three other patients are considered to have shown evidence of the arrest of vascular damage, but one died of adrenal insufficiency after leaving the authors' care. In the 2 other fatal cases the renal failure continued to

progress after operation, one patient dying from a cerebrovascular accident 4½ months after operation and the other from myocardial infarction 4 months after operation.

The authors are satisfied that there is ample evidence that the adrenal cortex plays a significant role in the aetiology of degenerative vascular disease in diabetes, and believe that total adrenalectomy has a place in the treatment of certain cases. Although the selection of cases for operation cannot be based on any single prognostic feature, in general the success achieved has been inversely proportional to the degree of vascular disease present. Patients with advanced renal failure should not be subjected to this form of treatment. *John Lister*

191. **Adrenalectomy in Human Diabetes. Clinical and Chemical Study of Bilateral Total Adrenalectomy in a Case of Advanced Intercapillary Glomerulosclerosis**
H. E. MARTIN and M. L. WILSON. *Diabetes* [*Diabetes*] 3, 375–382, Sept.–Oct., 1954. 15 refs.

The authors report the results of bilateral total adrenalectomy performed at the Los Angeles County Hospital (University of Southern California) on a woman of 28 who had had diabetes for 15 years and had signs of advanced vascular disease. These consisted in generalized oedema, extensive retinopathy, hypertension (180/100 mm. Hg), proteinuria (10 to 15 g. of protein in 24 hours), and a raised serum non-protein nitrogen level (77 mg. per 100 ml.). Vigorous treatment before operation reduced the oedema, the patient's weight falling from 183 to 160 lb. (83 to 72 kg.).

Bilateral total adrenalectomy was successfully performed, but a needle biopsy of the right kidney, carried out at the same time, provided evidence of severe intercapillary glomerulosclerosis. The patient was ambulatory within 3 days and was discharged after 3½ weeks. At this time she was taking 25 mg. of cortisone daily by mouth and 30 units of N.P.H. insulin, her blood pressure was 150/90 mm. Hg, and serum non-protein nitrogen level 50 mg. per 100 ml. For the next 4½ months the patient was well. However, because of a rise in serum potassium level and severe muscle aching the dose of cortisone was then increased to 50 mg. daily and an occasional small dose of deoxycortone acetate was given intramuscularly. With this treatment the blood pressure rose to 230/140 mm. Hg, intractable headaches occurred, and hypertensive retinal exudates reappeared, but on reducing the dose of cortisone to 25 mg. again both the hypertension and its manifestations were relieved. Weakness remained a disabling symptom, however, and 11 months after the operation the patient suddenly developed paralysis of the legs which rapidly spread to the arms, finally causing respiratory failure and death.

The authors are in no doubt that the patient died of adrenal insufficiency with hyperkalaemia and paralysis of the respiratory muscles. They stress the difficult therapeutic problem which arises after adrenalectomy, when the dose of cortisone necessary to relieve the adrenocortical insufficiency may be sufficient to give rise to signs of malignant hypertension. Although it was hoped that adrenalectomy might diminish the proteinuria in this case, there was no significant improvement in this respect except at one stage when the patient was in a state of mild adrenal insufficiency. Despite the fatal outcome in this case, the authors consider that adrenalectomy would be justifiable in similar cases with less advanced renal disease. *John Lister*

192. **Thyroid Stimulation in Diabetes Mellitus**
J. W. GODDARD and S. C. SOMMERS. *Diabetes* [*Diabetes*] 3, 383–388, Sept.–Oct., 1954. 2 figs., 7 refs.

Using the thyroid cell mapping method which they have previously described (*Lab. Invest.*, 1954, 3, 197) the authors have studied and compared the distribution in the thyroid glands of diabetics and non-diabetics of the four types of cell distinguished by Goormaghtigh and Thomas, each of which is said to have specific functional characteristics.

In necropsy specimens of thyroid tissue from 42 cases of diabetes mellitus, obtained from the files of the New England Deaconess Hospital, Boston, the outstanding finding was that in every case Type-II cells (which are thought to be responsible for the active reabsorption of follicular colloid and are prominent in cases of hyperthyroidism) were present in increased numbers. According to Goormaghtigh and Thomas this would indicate that increased secretory activity in the thyroid must be characteristic of diabetes. Some evidence was obtained that the high blood sugar level was a possible cause of this increase, since examination of thyroid tissue collected at necropsy from 13 non-diabetic subjects who had received intravenous glucose shortly before death revealed a similar increase in the number of Type-II cells.

On further analysis of the thyroid cell counts the 42 diabetic patients could be divided into two distinct groups, in one of which (containing 14 of the cases) Type-II cells made up more than 5% of the total count, whereas in the other group the proportion was 4·5% or less. (In the normal controls the average percentage of Type-II cells was 0·47.) These two groups showed no clinical differences, but the anterior lobe of the pituitary gland in cases of the former group was found to show distinctive histological changes, the basophil cells being increased in number and forming nodular or diffuse masses below the pituitary capsule, whereas in the latter group the appearances in the pituitary were normal.

The authors suggest, therefore, that in two-thirds of the diabetic patients studied the increase in thyroid activity was due to hyperglycaemia, whereas in the remaining one-third abnormal pituitary hyperactivity was responsible for causing active colloid reabsorption analogous to that found in hyperthyroidism.
John Lister

193. **A Form of Laënnec's Cirrhosis of the Liver Combined with Diabetes Mellitus, and its Relation to Haemochromatosis.** (Kombinationsformen von Laënnecscher Lebercirrhose mit Diabetes mellitus, ihre Beziehungen zur Hämochromatose)
A. REGLI. *Helvetica medica acta* [*Helv. med. Acta*] 21, 535–549, Dec., 1954. 2 figs., 13 refs.

The Rheumatic Diseases

194. **"Screening" of the Population for Rheumatic Diseases**
J. J. DE BLÉCOURT. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **13**, 338–340, Dec., 1954. 6 refs.

An investigation has been made of the incidence of rheumatic disease in a specified area of North Holland; 4,212 persons over the age of 14 were approached, and 3,378 (1,595 men and 1,783 women) came for interview; 621 (18·4%) were found to be suffering from some form of rheumatism, but most of these were not acutely affected at the time of the interview, the number seriously ill amounting to 1·35% of the 3,378 examined. Articular complaints accounted for 44·7% and muscular pains for 55·3% of those affected. The proportions of men and women affected were 13·5 and 21·7% respectively; 84·5% of the men and 79·1% of the women were over 40 years of age.

These results are compared with those of other investigators in Denmark, England, and Sweden.—[Author's summary.]

195. **Muscle Spasm as a Cause of Somatic Pain**
D. TAVERNER. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **13**, 331–335, Dec., 1954. 5 figs., 10 refs.

In a study carried out at the University of Leeds the author has examined the evidence on which the concept of muscular spasm as a common cause of pain is based, starting from the observation that some painful muscles are both tender and firm to the touch. Elliot (*Lancet*, 1944, **1**, 47) demonstrated by electromyography that the tender muscles of patients suffering from prolapsed intervertebral disk showed increased irritability and sometimes also spontaneous electrical activity. He referred to these electrical changes as "muscle spasm", and suggested that this may cause pain either because unphysiological muscular contraction is painful or because muscles contracting under ischaemic conditions become painful.

In criticizing this suggestion the present author points out that it is one of the minor problems of electromyography to produce the complete muscle relaxation which is necessary to achieve electrical silence. The insertion of a needle into a tender muscle is likely to provoke involuntary muscle contraction, and the discovery of single motor units firing spontaneously does not necessarily prove that there has been pre-existing spontaneous muscular activity. Spontaneous electrical activity is seen in such painless conditions as amyotrophic lateral sclerosis and dystrophia myotonica. Painful cramp is characterized by sustained electrical activity at frequencies of 300 per second or more, a frequency never achieved in the most intense voluntary contraction. The author has never seen spontaneous activity suggestive of cramp in other painful conditions. He has noticed an abnormal degree of electrical activity in the erector spinae muscles in acute lumbago which appeared when the patient made the slightest movement, but when fully relaxed the muscles became electrically silent although pain persisted. He describes the result of electromyography in a woman patient who suffered from severe pain in the right trapezius muscle brought on by knitting. No abnormal electrical activity was observed in either of the trapezius muscles during knitting; moreover, both muscles were electrically silent after a spell of knitting, when the pain was severe. The author therefore concludes that there is very little reliable evidence in support of the theory that muscle spasm is a direct cause of somatic pain. *C. E. Quin*

See also Pathology, Abstract 1.

ACUTE RHEUMATISM

196. **Changing Status of Rheumatic Fever and Rheumatic Heart Disease in Children and Youth**
H. M. WALLACE and H. RICH. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **89**, 7–14, Jan., 1955. 5 figs., 10 refs.

The authors have found few reports in the American literature which substantiate or refute the claim that there has been a change in recent years in the picture of rheumatic fever and rheumatic heart disease in children and young adults. In this paper they discuss the mortality from these two conditions as recorded in New York City over the 11-year period 1940–50 and the incidence of heart disease in children in the years 1943 and 1952.

In the period under review there was a significant reduction in the number of deaths from rheumatic heart disease in children and young adults under the age of 20, especially in white children. In 1952, as compared with 1943, fewer children had heart disease of rheumatic origin and it was noted that a higher proportion were placed in ordinary schools as opposed to special schools, indicating, presumably, freedom from cardiac disease. In the 11-year period 1940–50 there was a 74% decrease in mortality from rheumatic fever in the age group 0 to 20 years. *R. S. Illingworth*

197. **Group A *beta*-Hemolytic Streptococci and Rheumatic Fever in Miami, Fla.**
M. S. SASLAW and M. M. STREITFELD. *Public Health Reports* [*Publ. Hlth Rep. (Wash.)*] **69**, 877–882, Sept., 1954. 15 refs.

Because of the reported low incidence of rheumatic heart disease, polyarthritis, and chorea and the lessened severity of these diseases in the warm southern parts of the United States, the authors have investigated the incidence of Group-A β-haemolytic streptococci in the throats of 343 healthy children attending three schools

in Miami, Florida. In most cases duplicate swabs were taken at monthly intervals between February and May 1953, but in some more than two were taken, the average number for the whole group being 3·4. The children were selected to represent different racial groups and socio-economic levels. One swab was cultured on " difco " blood-agar base enriched with 4% defibrinated sheep's blood, and the others on various media in an attempt to assess the relative value of different media. Brewer's thioglycollate broth (" difco ") and neopeptone heart-infusion agar (difco) containing 4% defibrinated sheep blood both proved valuable in recovering additional strains [but there is no evidence that such strains might not have been cultured from a second swab on the first medium]. Grouping and typing by the Lancefield precipitin method was performed, the latter for 36 types. In all, 59 strains of Group-A β-haemolytic streptococci were isolated from 47 children. All of the 27 typable strains were of Type 12 with one exception, which was Type 28. In 14 instances repeated cultures were positive. Of the 343 children observed over the 4-month period, 16·3% gave cultures of Group-A β-haemolytic streptococci; this compares with a figure of between 5 and 10% reported by Denny for normal children. No anti-streptolysin-O titres were performed. There was no complete follow-up of all illnesses during the period of study, but none of the children was admitted to hospital for acute rheumatic fever or frank nephritis.

E. G. L. Bywaters

CHRONIC RHEUMATISM

198. **Acrylic Arthroplasty in Ankylosing Spondylitis.** (L'arthroplastie acrylique dans la spondylarthrite ankylosante)

R. M. D'Aubigné, J. O. Ramadier, and M. Postel. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **22**, 16–24, Jan., 1955. 3 figs.

The authors review the results of operations designed to increase the mobility of hip-joints ankylosed as a result of extension of ankylosing spondylitis. They urge [with justification] that in patients with a combination of ankyloses of the spine, hip, and often also one or both knees, any effort made to restore some degree of movement at least to the hip- and knee-joints is worth while, since without such attempts the patients are for all practical purposes helpless, having the choice of only two positions, the horizontal and the upright; they cannot change position without assistance, cannot sit, and can usually walk only with extreme difficulty with the aid of crutches.

The authors have so far performed arthroplasty on 38 occasions on 21 patients, but the results in only 14 who were subjected to bilateral operation are discussed here. In 17 operations the Judet-type of prosthesis was employed, but the best results were obtained with the use of a special type of acrylic prosthesis for the head and neck of the femur which has a long intramedullary stem. In 13 of the 14 patients increased mobility of the hip-joints, ranging from 36 to 43 degrees, was achieved, all 13 could walk more easily, and 12 could sit down unaided; 3 of the patients have been able to resume their former employment. The special hazard of the operation is hyperaemia, which makes good haemostasis difficult. The extensive changes which occur in the soft parts around the joints, such as deposit of fat and matting of the fascial planes in every layer, are described. The authors believe that preoperative exercise of the legs carried out in bed may prevent these changes, a crucial factor in these cases, from developing fully. In 4 cases they tried excision of the head and neck of the femur without fitting a prosthesis, but the results were less satisfactory.

L. Michaelis

199. **Local Anti-rheumatic Effectiveness of Higher Esters and Analogues of Hydrocortisone**

J. L. Hollander, E. M. Brown, R. A. Jessar, L. Udell, N. Smukler, and M. A. Bowie. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **13**, 297–301, Dec., 1954. Bibliography.

The alleviating effect of the intra-articular injection of hydrocortisone acetate into arthritic joints is undoubted, but the transitory nature of the improvement is a serious drawback. Investigations into the disappearance of the compound from the synovial fluid after injection have revealed that some of the hormone is absorbed into the synovial membrane without splitting of the ester, whereas unabsorbed hormone in the joint fluid is rapidly hydrolysed and broken down. On the assumption that higher and less soluble esters would likewise be absorbed unchanged by the synovial membrane and might have a longer anti-inflammatory effect the authors, working at the Hospital of the University of Pennsylvania, Philadelphia, have compared the degree and duration of benefit derived from injection of hydrocortisone acetate with that from other preparations of hydrocortisone in the knee-joints of patients suffering from osteoarthritis and rheumatoid arthritis. The other preparations used were 9-α-chlorohydrocortisone, *allo*-dihydrohydrocortisone, hydrocortisone tertiary butyl acetate, hydrocortisone caprylate, and hydrocortisone benzoate. All comparisons were based on identical doses.

The tertiary butyl acetate was compared with hydrocortisone acetate in 171 cases, and was found to be more effective in relieving symptoms and signs in 65% of cases, equally effective in 30%, and less effective in 5%. The duration of benefit was increased by at least 3 days in 59% of cases, was of equal length in 35%, and was shorter in 6%. The other compounds were tried on only 17 patients. 9-α-Chlorohydrocortisone produced an average of 8 days' relief compared with 6 days for hydrocortisone acetate, the *allo*-dihydro compound produced alleviation for an average of one day, the caprylate was little better than hydrocortisone acetate, while the duration of relief with the benzoate averaged 8 days in 9 cases; further trial had, however, to be abandoned because of the high incidence of post-injection reactions.

9-α-Fluorohydrocortisone was also tried in doses of 5 mg., but produced results no better than hydrocortisone acetate in the usual dosage. When the dose

was increased to 7·5 mg. in one knee or to 5 mg. each in both knees marked oedema of the legs appeared. As the authors pertinently remark, this latter effect would seem to nullify the advantage of increased dosage.

C. E. Quin

200. **Action of Hydrocortisone on the Hyaluronic Acid of Joint Fluids in Rheumatoid Arthritis**

L. SUNDBLAD, N. EGELIUS, and E. JONSSON. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **6**, 295–302, 1954. 2 figs., 21 refs.

At the Södersjukhus, Stockholm, the synovial fluid from the knee-joints of 14 patients with active rheumatoid arthritis was examined before and 2 to 3 days after the intra-articular injection of 50 mg. of hydrocortisone acetate. The joints were not emptied completely, but the degree of effusion was calculated by a dilution method.

It was found that the beneficial local effect of intra-articular injection of hydrocortisone was always accompanied by biochemical changes in the joint fluid, and that the converse applied in a few cases in which " butazolidin " (phenylbutazone) or a synthetic hyaluronidase inhibitor was similarly administered. There was a rise in hyaluronic acid concentration in the majority of cases, but the most consistent change was an increase in the degree of polymerization of hyaluronic acid, as manifested by a rise in both the intrinsic viscosity and the degree of anomaly of flow; in about half the cases the intrinsic viscosity rose to normal. In a few cases in which repeated aspiration was carried out the maximum response occurred after 2 to 4 days. The volume of the effusion decreased from an average of 20 ml. to an average of 4 ml.

A slight but significant decrease in hyaluronidase-inhibitor activity of the fluids was observed after intra-articular administration of hydrocortisone, and the authors therefore suggest that the changes in the hyaluronic acid cannot be ascribed to inhibited depolymerization. In their view the hormone probably acts directly or indirectly on the synovial tissue, where the hyaluronic acid is presumably synthesized.

J. Warwick Buckler

201. **The Effects of Aldosterone (Electrocortin) and of 9α-Fluorohydrocortisone Acetate on Rheumatoid Arthritis: Preliminary Report**

L. E. WARD, H. F. POLLEY, C. H. SLOCUMB, P. S. HENCH, H. L. MASON, V. R. MATTOX, and M. H. POWER. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **29**, 649–663, Dec. 22, 1954. 7 figs., 30 refs.

Aldosterone and 9-α-fluorohydrocortisone acetate, 2 recently discovered steroids, were administered at the Mayo Clinic to a number of patients with rheumatoid arthritis, and the authors here report the clinical and metabolic effects observed.

Aldosterone, derived from animal adrenal tissue, was administered to 2 patients by intramuscular injection for 6 days each. The daily dose in the first case was 800 μg., and in the second 1,000 μg. These doses had no anti-rheumatic effect on either patient, but did produce some retention of sodium, chloride, and fluid, as would be expected. 9-α-Fluorohydrocortisone acetate, a synthetic product, was administered to 3 patients in doses of 4 mg., 6 mg., and 8 mg. respectively daily for 12 to 28 days. With these moderate doses rheumatic symptoms were lessened, but troublesome retention of sodium, chloride, and fluid was produced and potassium loss was increased. Oedema and signs of hypopotassaemia appeared, and a tendency was noticed also towards the development of hypochloraemia and alkalosis.

Despite the apparent lack of antirheumatic activity of aldosterone and the obvious therapeutic limitations placed on 9-α-fluorohydrocortisone acetate by its side-effects, the authors consider that the fact that such marked differences in characteristics and potency exist between these and other steroid substances of natural or synthetic origin strongly suggests that superior compounds will in due course be developed for the control of the clinical course of rheumatoid arthritis, and so render its management easier.

W. S. C. Copeman

202. **Preliminary Clinical Trials with 9-*alpha*-Fluorohydrocortisone Acetate in Rheumatoid Arthritis**

E. W. BOLAND and N. E. HEADLEY. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **13**, 291–296, Dec., 1954. 7 refs.

The authors draw attention to the results of animal experiments with halogenated derivatives of hydrocortisone which have shown that these compounds possess unusually high glycogenic activity. Compared with deoxycortone acetate, 9-α-fluorohydrocortisone acetate is about ten times more potent in respect of glycogenic activity and is more potent in producing involution of the thymus gland and sodium retention. The compound has also been found to be highly efficacious, in doses as small as 0·25 to 1 mg. daily, in maintaining patients with Addison's disease.

In the present study, carried out at the University of California, Los Angeles, the clinical response to orally administered 9-α-fluorohydrocortisone acetate was observed in 13 patients with active rheumatoid arthritis. Of these patients, 7 had had no previous hormone therapy and 3 of this group were later transferred to treatment with hydrocortisone (free alcohol) in order to allow of dosage comparisons. The remaining 6 patients, who had been receiving hydrocortisone, were transferred directly to the new compound, the difference in dosage requirements being noted.

With total initial doses ranging from 4 to 8 mg. per day subjective and objective improvement was recorded in 5 of the 7 patients, and the degree and speed of over-all improvement compared favourably with that which would have been expected from treatment with cortisone or hydrocortisone in much larger doses. A comparison of the maintenance-dosage requirements for the new compound and hydrocortisone was made in 9 patients, and showed that the antirheumatic potency of 9-α-fluorohydrocortisone acetate was very nearly 10 times greater than that of hydrocortisone (free alcohol).

Two adverse reactions to 9-α-fluorohydrocortisone were prominent, namely, fluid retention and elevation of the blood pressure, the former being noted in 12 and the latter in 6 of the 13 patients. When a transfer to equally effective amounts of hydrocortisone was made, signs of fluid retention disappeared within 2 to 5 days and the blood pressure returned to its former level in 4 to 14 days. One patient developed a low-grade fever and another albuminuria and cylindruria after 2 weeks' medication with the new compound, but these effects also disappeared on transfer to hydrocortisone.

The authors conclude that the powerful salt- and water-retaining properties of 9-α-fluorohydrocortisone acetate will probably prohibit its employment as a systemic medication for rheumatoid arthritis.

C. E. Quin

203. **Studies on Metacortandralone and Metacortandracin in Rheumatoid Arthritis. Antirheumatic Potency, Metabolic Effects, and Hormonal Properties**
J. J. Bunim, M. M. Pechet, and A. J. Bollet. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **157**, 311–318, Jan. 22, 1955. 7 figs., 4 refs.

Metacortandralone and metacortandracin, two new synthetic steroids, were tried in the treatment of 7 patients with rheumatoid arthritis, in all of whom conventional treatment had been unsuccessful and 4 of whom had given no response to cortisone. The investigation was concerned mainly with metacortandralone, the authors stating that metacortandracin appeared to be very similar in action and potency.

Metacortandralone was given by mouth in an initial suppressive daily dose of 30 to 60 mg.; this was later reduced to a maintenance dose varying from 5 to 25 mg. daily. None of the patients was aware of the change in treatment from salicylates or cortisone to metacortandralone. Subjective improvement was noted within 4 to 6 hours of administration of the first dose of metacortandralone and was obvious within 24 hours; objective improvement was more gradual, being greatest after 2 to 3 weeks. There was consistent improvement in joint inflammation, indicating that the drug possessed antirheumatic properties, and this was confirmed in 3 patients by histological examination of biopsy specimens of the synovial membrane taken before and during treatment, a striking subsidence of inflammation being noted. Side-effects were not serious, and disappeared when the dose was reduced to maintenance level. In 2 patients signs and symptoms of arthritis returned within about 2 weeks of withdrawal of the drug; no other constitutional symptoms were noted. In the 4 cases in which there had been no response to cortisone the maintenance dose of metacortandralone appeared to be from one-third to one-fifth of that of cortisone, but this estimate, the authors point out, may require revision after more experience has been gained.

Administration of metacortandralone resulted in a prompt and uniform fall in the eosinophil count and a reduction in the urinary excretion of 17-ketosteroids. A rise in the serum cholesterol level was observed in 6 cases. Carbohydrate metabolism appeared to be unaffected, and no change was observed in the sodium or potassium balance with a dose of 30 mg. daily; 50 mg. daily was necessary to induce a negative nitrogen balance.

The authors conclude that these synthetic steroids are several times more potent than cortisone, and that this potency does not appear to be accompanied by an increase in the severity of side-effects. They emphasize, however, that a long-term investigation is necessary to determine their true value. *B. E. W. Mace*

204. **Observations on 69 Cases of Rheumatoid Arthritis Treated with Di-(2-chloroethyl)-methylamine Hydrochloride.** (Quelques considérations sur 69 cas de polyarthrite chronique evolutive traités par le chlorhydrate de méthyl-bis-β-chloroéthyl-amine)
A. Robecchi, F. Cartesegna, and V. Daneo. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **21**, 823–828, Dec., 1954.

At the Rheumatological Centre, Turin, 69 patients (20 men and 49 women), of whom 62 had rheumatoid arthritis and 5 " psoriatic rheumatism ", were given a dose of 5 mg. of nitrogen mustard intravenously either on alternate days or every third day; after 4 injections there was an interval of 8 to 20 days and then another 4 injections completed the course. In the rheumatoid arthritic patients the results were " excellent " in 19%, " satisfactory " in 47·5%, " insignificant " in 17·5%, and there was no benefit in 16%. Neither sex nor age appeared to influence the results, and if the first course of treatment failed no benefit was derived by repeating it. The cases of psoriatic rheumatism reacted in much the same way as rheumatoid arthritis in so far as the joint condition was concerned, and the skin lesions cleared in one case. But treatment had to be interrupted in 4 of the 5 cases because of persistent vomiting. In the group of patients with rheumatoid arthritis, however, side-effects were few.

[In most of these cases the treatment was followed by a standard course of gold or cortisone; it is therefore difficult to assess the long-term effects of the nitrogen mustard. Nevertheless, the authors claim that one patient with rheumatoid arthritis who reacted very well to a course of nitrogen mustard was still in " satisfactory condition " one year later having, in the intervening period, been maintained on 37·5 mg. of cortisone daily.]

David Preiskel

205. **Rhematoid Arthritis and Polyarteritis Nodosa.**
J. Ball. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **13**, 277–290, Dec., 1954. 14 figs., 33 refs.

Clinical and necropsy findings are presented in 5 cases, illustrating the association of rheumatoid arthritis and polyarteritis nodosa. In 4 of these, disseminated arteritis apparently complicated an established and typical rheumatoid process, the pathogenesis of the arthritis being essentially independent of the arterial lesions. In one case the arteritis was an incidental finding, in the others it was a major contributory cause of death. Only one of the 4 cases had received cortisone; none had received ACTH. In the fifth case a short arthritic episode occurred in an illness diagnosed clinic-

ally and histologically as polyarteritis nodosa; at necropsy the joints showed typical rheumatoid changes in the absence of articular arteritis.

It is suggested that, though polyarteritis nodosa is a rare complication of rheumatoid arthritis, the association of these two conditions is more than coincidental. The available evidence suggests that the distribution, frequency, and morphology of arterial lesions in rheumatoid arthritis are variable, ranging from a mild indeterminate arteritis to classical polyarteritis nodosa.—[Author's summary.]

206. **Failure of Skin Testing to Detect Antigen–Antibody Properties in the Tissues of Rheumatoid Arthritis**
J. LANSBURY, G. E. ALLEN, and F. B. ROGERS. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 191–192, Feb., 1955. 2 refs.

The authors report on reactions to intradermal injections of test material derived from joint fluid, joint synovium and rheumatoid nodule of 3 patients with typical rheumatoid arthritis. The three test materials and a control material derived from *E. coli* filtrate were administered to a series of 20 cases of rheumatoid arthritis and a series of 20 non-rheumatic control patients. All cases gave a moderate response to the bacterial filtrate. None gave any local or systemic response to the filtrates of rheumatoid tissue. It is concluded that those features of rheumatoid arthritis which suggest antigen–antibody reaction may lie in the field of some as yet unknown immune mechanism.—[Authors' summary.]

207. **Auto-antibodies in Rheumatoid Arthritis. A Simple Method of Demonstration with Possible Diagnostic Application.** (Autoanticuerpos en la poliartritis crónica progresiva. Método sencillo de demostración con posibles aplicaciones diagnósticas)
A. FOZ, E. BATALLA, and L. ESPACIO. *Revista de diagnostico biologico* [*Rev. Diagn. biol. (Madr.)*] **3**, 460–470, Nov.–Dec., 1954. 6 refs.

The similarity between the Coombs test for incomplete antibodies and the Waaler–Rose test for rheumatoid arthritis suggests that the rheumatoid-arthritis serum (R.A.S.) factor may be an auto-antibody against the patient's own globulin. The erythrocytes act passively as a carrier of the globulin and can be replaced by other carriers, such as erythrocytes of other species. In studies carried out at the Municipal Hospital for Infectious Diseases, Barcelona, the authors have used a system of *Brucella abortus* sensitized with human incomplete anti-*Brucella* antibody for detection of the R.A.S. factor. The human anti-*Brucella* serum had an agglutinin titre of 1 in 15 and an incomplete antibody titre of 1 in 2,500. A washed, killed suspension of *Br. abortus* was sensitized by incubation for one hour at 37° C. with this serum diluted to a titre of 1 in 125. In performing the test the patient's serum is diluted with saline in successively doubled dilutions in ten tubes, 0·5 ml. of each dilution is added to 0·5 ml. of sensitized *Brucella* suspension, and the mixture incubated at 37° C. Agglutination is judged visually. A control series of dilutions is set up, using a suspension of unsensitized *Br. abortus*. If the test serum contains *Brucella* antibodies, they are removed by absorption.

The test was carried out on 54 healthy control subjects and 23 patients with rheumatoid arthritis. In 19 of the latter, antibody titres ranged from 1 in 80 to 1 in 10,240; in one case the titre was 1 in 40, in another the test result was doubtful, and in 2 cases it was negative. Only one of the 54 control subjects gave a positive test result (titre 1 in 320). The Waaler–Rose test was negative in 5 of the cases of rheumatoid arthritis. The authors report that they are using with success a system of Rh-positive erythrocytes sensitized with incomplete Rh-antibodies [but give no details]. *M. Lubran*

208. **Determination of Anomalous Viscosity in Pathological Joint Fluids**
L. SUNBLAD. *Scandinavian Journal of Clinical and Laboratory Investigation* [*Scand. J. clin. Lab. Invest.*] **6**, 288–294, 1954. 2 figs., 13 refs.

The author, working at Södersjukhuset, Stockholm, describes a method for determining the degree of anomalous viscosity in synovial fluid. [The original paper must be studied for technical details.] While the degree of correlation between anomalous and intrinsic viscosity was fairly high at a chosen stress, the presence of even a small fraction of highly polymerized hyaluronic acid caused marked anomalies in flow, whereas the intrinsic viscosity was less affected. The author therefore suggests that determination of anomalous viscosity is of more value than determination of intrinsic viscosity for detecting the presence of highly polymerized fractions of hyaluronic acid in pathological fluids—for example, fluids which occur in rheumatoid arthritis after treatment with hydrocortisone (*Scand. J. clin. Lab. Invest.*, 1954, **6**, 295).

Since no quantitative estimation of hyaluronic acid is required the method could thus be used as a clinical test for degradation of hyaluronic acid in pathological fluids. The author also suggests that the determination of anomalous viscosity may be of value in studying hyaluronic acid changes when other mucopolysaccharides are present—for example, in connective-tissue extracts. *J. Warwick Buckler*

209. **Osteo-arthritis Deformans of the Luschka Joints**
A. J. E. CAVE, J. D. GRIFFITHS, and M. M. WHITELEY. *Lancet* [*Lancet*] **1**, 176–179, Jan. 22, 1955. 4 figs., 12 refs.

The authors, discussing the possible causes of cervicobrachial neuritis, state their belief that protrusion of the cervical intervertebral disks is less frequently responsible than deforming osteoarthritis of the neurocentral joints of Luschka. They base this opinion on their findings in an anatomical study of 60 adult cervical spines carried out at St. Bartholomew's Hospital Medical College, London, and describe 12 unselected cases of cervicobrachial neuritis in out-patients attending the hospital, in all of whom they demonstrated the condition radiologically. The suggested mechanism is a compression angulation of the contents of the intervertebral canals by bony encroachment on to their medial end.
A. C. Lendrum

Physical Medicine

210. **Comparison of Ultrasonic and Microwave Diathermy in the Physical Treatment of Periarthritis of the Shoulder**
J. F. LEHMANN, D. J. ERICKSON, G. M. MARTIN, and F. H. KRUSEN. *Archives of Physical Medicine and Rehabilitation* [*Arch. phys. Med.*] **35**, 627–634, Oct., 1954. 5 figs., 48 refs.

The authors review reports in the literature of the results of treatment of periarthritis of the shoulder by ultrasonic irradiation. They consider the effect of such treatment to be due purely to the heat generated, but they give their reasons for considering that ultrasonic therapy raises the temperature selectively in the fibrous capsule, the tendons, and possibly the nerves in the region of the shoulder-joint. At the Mayo Clinic, 78 patients with periarthritis of the shoulder were treated with ultrasonic radiation and 78 with microwave diathermy. Both groups were told that they were receiving "diathermy", and received the same subsequent treatment with massage and exercises. Improvement was estimated by measuring the amount of increase in range of movement after treatment. A very critical statistical survey of the results was made, which showed a significantly greater improvement in the group treated with ultrasonic waves.

The authors do not accept these results at their face value, pointing out that the degree of superiority of ultrasonic therapy over microwave diathermy was not established. They consider that in the hands of a skilled physician ultrasonic therapy can be useful in the treatment of periarthritis of the shoulder, perhaps in combination with other types of treatment. There are, however, certain dangers in, and contraindications to, ultrasonic therapy, and in view of these it is debatable whether this form of treatment should be used in preference to any other which will give comparable results.
W. Tegner

211. **Electrical Investigations in the Diagnosis of Lumbar and Sciatic Pain.** (L'examen électrique dans le diagnostic des lombo-sciatalgies)
A. ROBECCHI and E. BARBASO. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **21**, 817–822, Dec., 1954.

The conception that sciatica is due to protrusion of an intervertebral disk makes it important to discover which nerve-root is affected. To do this the authors have used faradic stimulation of muscles, carried out by means of an electrode terminating in a round plate about 2 cm. in diameter and fitted with a suitable current interruptor. For examining the back muscles the patient is placed in the prone position and the indifferent electrode applied to the abdomen: for examination of anterior or lateral muscles the supine position is assumed, the indifferent electrode being placed on the buttock. The patient is asked to relax as much as possible, and the response obtained is classed as normal, exaggerated, or diminished. They have found that hyperexcitability is frequently seen in mild sciatica or at the beginning of an attack, whereas diminution or disappearance of excitability is more likely to be met with in severe or long-standing sciatica.

In the authors' experience, motor involvement is more common than sensory loss. Of 122 cases recently observed at the Rheumatological Centre, Turin, it was found that sciatica due to protrusion of the 5th lumbar disk accounted for 52 cases, and of the first sacral disk for 70. There was remarkable agreement between the results of electrodiagnosis and those of other methods in defining the site of the protrusion, but in a number of cases of radiculitis at the level of S1 the electrical findings were normal in the presence of a diminished or absent ankle-jerk; the authors explain this discrepancy on the basis of sensory involvement. They advise the routine use of electrodiagnosis in sciatica, but admit that owing to various anatomical variations there may be an error of 9%.
David Preiskel

212. **Orthopaedic Treatment of Coxarthroses**
H. MILCH. *Archives of Physical Medicine and Rehabilitation* [*Arch. Phys. Med.*] **36**, 93–98, Feb., 1955. 5 refs.

213. **Posture and the Resting State**
W. BARLOW. *Annals of Physical Medicine* [*Ann. phys. Med.*] **2**, 113–122, Oct., 1954. 15 figs., 14 refs.

The central problem in postural re-education is the detection of postural error. The physiological basis for the detection of "error" in muscle tension is described with reference to recent work on the small-nerve innervation of the muscle spindle. A concept of the "resting state", based on the servo- or feedback mechanism of the muscle spindle, is outlined and related to the general problem of postural homoeostasis. In view of the fact that muscle shortening interferes with spindle activity, any form of re-education which involves a contraction of muscle will not assist in the patient's detection of error. Specific remedial exercises as at present practised mostly impair rather than improve the patient's ability to detect errors in muscle tension. These points are illustrated by electromyographic and photographic records, and a method of re-educating the postural sensibility by a conditioning procedure is outlined.

It is tentatively suggested that muscle "priming" preparatory to activity is a function of the small-nerve system, and that psychological maladjustments in which excessive muscle tension plays a part may be tackled by teaching the subject to prepare for activity by mental "priming" rather than by muscular contraction. By this means postural awareness is maintained and the patient is able to return to a resting state of tonus after activity. The need to subject present methods of muscular re-education to a strict inquiry is emphasized. —[Author's summary.]

Neurology and Neurosurgery

214. **Landry–Guillain–Barré Syndrome: Cardiovascular Complications. Treatment with A.C.T.H. and Cortisone**
E. CLARKE, R. I. S. BAYLISS, and R. COOPER. *British Medical Journal* [*Brit. med. J.*] **2**, 1504–1507, Dec. 25, 1954. 2 figs., bibliography.

After briefly reviewing earlier papers containing references to cardiovascular complications of the Landry–Guillain–Barré syndrome the authors describe 3 cases of the syndrome seen at Hammersmith Hospital, London, in each of which there was circulatory collapse with hypotension. The first patient, a woman aged 63, died 6 days after admission, but post-mortem examination showed no abnormality of the myocardium apart from some hypertrophy due to pre-existing hypertension. In the second case, in a man of 45, there were hyperkalaemia and hyponatraemia, possibly due to acute adrenal insufficiency; in this case both the nervous and cardiovascular symptoms improved promptly when cortisone and digoxin were administered. The third patient, a man aged 30, was admitted complaining of back pain, headache, and stiffness of the neck. Weakness of the muscles developed rapidly and it became necessary to aid respiration. In this case the cardiovascular collapse was accompanied by a pericardial friction rub and a recrudescence of the muscle weakness.

The symptoms and treatment of these cases are discussed. In the authors' opinion the circulatory collapse was due to myocardial involvement and not to loss of peripheral vascular tone. They suggest that treatment should include infusion of noradrenaline to combat the hypotension, together with digoxin and cortisone in the hope that these may improve the myocardial function and perhaps favourably influence the pathological process. *L. G. Kiloh*

215. **Neurologic Diseases on the Island of Guam**
D. W. MULDER, L. T. KURLAND, and L. L. G. IRIARTE. *United States Armed Forces Medical Journal* [*U.S. armed Forces med. J.*] **5**, 1724–1739, Dec., 1954. 5 figs., 21 refs.

Previous surveys have shown that amyotrophic lateral sclerosis is very much more prevalent among the inhabitants of the island of Guam in the Western Pacific than in the U.S.A. or in Europe. The mean age at onset is about 44 years, and the median period of survival is estimated at 3 years; the disease is similar in all respects to amyotrophic lateral sclerosis as encountered elsewhere. From a house-to-house survey of a large part of the island the incidence of the disease was estimated at 400 per 100,000, about 1% of all adults over the age of 20 being affected; 4% of all deaths on Guam are due to the disease. The incidence is highest in Umatac, an isolated village in which sanitary conditions are worse than anywhere else on the island; here between one-quarter and one-third of all adult deaths are due to the disease. In other parts of the island, too, amyotrophic lateral sclerosis tends to be more frequent among the poorer classes, suggesting that exogenous factors play some part in the pathogenesis of the disease. However, the disease also occurs among those inhabitants living in the best sanitary conditions and among emigrants from Guam, whereas it is almost absent in the transient Filipino population. It seems likely, therefore, that hereditary factors are of considerable importance—the population of Umatac is extensively inbred—and the low social status of the majority of patients may be the result of the disease recurring through several generations rather than its cause.

Of other neurological diseases, post-encephalitic Parkinsonism is relatively common, whereas disseminated sclerosis and cerebral tumours are virtually non-existent. Cerebral vascular disorders are relatively uncommon, and poliomyelitis and leprosy are now rare. [Polyneuritis is not mentioned.] *J. Foley*

BRAIN AND MENINGES

216. **Decerebrate State in Children and Adolescents**
R. C. L. ROBERTSON and C. POLLARD. *Journal of Neurosurgery* [*J. Neurosurg.*] **12**, 13–17, Jan., 1955. 1 ref.

Though little distinction is usually made between the decerebrate and the decorticate states in clinical practice, most of the patients with what is known as decerebrate rigidity are probably in the decorticate state, and nearly all have one or more associated lesions of the brain. The present report from Baylor University Medical College, Houston, Texas, describes the fate of an unselected series of 26 patients, 13 adults and 13 children and adolescents, in all of whom more or less complete rigidity was present. The numbers are too small for the results to be of statistical significance, but in view of the usual association of a more or less hopeless prognosis with the clinical signs of decerebrate rigidity they are considered to be of definite interest.

Of the 13 children and adolescents, 4 died, but 6 recovered completely and are relatively normal neurologically, whereas none of the 6 adults who survived, and who showed similar decerebrate signs, are normal. So far as can be ascertained, the intellectual level of all the children who survived is normal for their age, and certainly none is a neurological wreck, whereas post-decerebrate vegetation is all too common in adults. None of the adult survivors has been able to return to work, and only 2 can feed and dress themselves. The immediate mortality (within 4 days of the trauma) among the children was the same as among the adults, and it is evident that the decerebrate state, especially in the younger child, is a very dangerous condition. The intensity of neurological signs is not necessarily related to mortality, since several patients in this series with com-

paratively mild signs died, whereas 3 children with severe signs made a complete recovery.

Tracheotomy is strongly advocated in those cases in which the respiratory tract cannot easily be kept free of secretion by postural drainage and suction. Delay in performing this operation may well add to the permanent neurological deficit if it results in repeated episodes of hypoxia and cyanosis. *D. P. McDonald*

217. **The Influence of Shock on Cerebral Hemodynamics and Metabolism**

J. F. FAZEKAS, K. KLEH, and A. E. PARRISH. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **229**, 41–45, Jan., 1955. 4 refs.

At the District of Columbia General Hospital, Washington, D.C., the cerebral blood flow was measured in 11 patients suffering from shock, the method employed being that of Kety and Schmidt using nitrous oxide. The underlying causes of the shock varied widely, but in all cases there was a low arterial blood pressure, ranging from 20 to 76 mm. Hg (mean 51 mm. Hg); 9 of the patients were comatose or stuporose.

It was found that in all cases the cerebral blood flow in ml. per 100 g. brain per minute was reduced considerably below normal, the mean value being 31·5 compared with normal values of 57·5 for young subjects and 47·7 for the elderly. The cerebral vascular resistance was raised, but not significantly so. The mean value for the cerebral metabolic rate was markedly less than normal. The arterial oxygen content was low in most cases, but in spite of this the arterio-venous oxygen difference was often greater than normal since the venous oxygen content was extremely low in some cases. In a few cases, including the 2 patients who were still conscious, the reduced cerebral blood flow appeared to be compensated for by a great increase in extraction of oxygen from the blood by the brain. Where this compensation was not present it is suggested that irreversible damage to the cerebral cells had occurred, an important consideration in determining the probable prognosis.

Donald McDonald

218. **The Treatment of Subacute and Chronic Subdural Haematomas**

R. G. ROBINSON. *British Medical Journal* [*Brit. med. J.*] **1**, 21–22, Jan. 1, 1955. 7 refs.

It is first pointed out that some of the poor results obtained in the treatment of chronic subdural haematoma are due to failure of the brain to expand after the haematoma fluid has been aspirated. The method of treatment used in 28 cases of subacute and chronic subdural haematoma at Dunedin Hospital is then described. The ages of the patients ranged from 17 to 77 years, and the interval between head injury and the development of the haematoma varied between 7 and 21 days.

Analysis of the clinical features did not disclose anything new or unusual. In 8 cases the patient's condition had been made worse by previous lumbar puncture, and the danger of this procedure is emphasized. The diagnosis was confirmed by angiography, and this was followed by burr-hole exploration under local analgesia. The subdural space was irrigated until the returning fluid was clear. This procedure was used in 14 cases; in the other 14, in which the brain was seen to be sunken after aspiration of the haematoma, Ringer's solution was injected by lumbar puncture until the brain expanded, 50 to 200 ml. of solution usually being required for this purpose. After-treatment consisted in keeping the patient in the supine position and maintaining a good fluid intake. Lumbar puncture was carried out daily and if cerebrospinal-fluid pressure was below 150 mm. H_2O, Ringer's solution was injected to raise the pressure to that level. It was found that with this method consciousness returned more rapidly, headache was relieved, and recurrence was prevented. In some cases expansion was carried out by direct ventricular injection, but this is a more difficult procedure than lumbar puncture and has no advantages. *Brodie Hughes*

219. **A New Method of Treatment of Inoperable Brain Tumours by Stereotaxic Implantation of Radioactive Gold—a Preliminary Report**

J. TALAIRACH, G. RUGGIERO, J. ABOULKER, and M. DAVID. *British Journal of Radiology* [*Brit. J. Radiol.*] **28**, 62–74, Feb., 1955. 12 figs.

The authors describe their experience at the Hôpital Ste Anne, Paris, in the treatment of 5 cases of intracranial neoplasm by the implantation of radioactive gold by a stereotaxic method [which is not described] after accurate location of the lesion. Of the 5 patients treated, one had a tumour in the posterior part of the third ventricle and was well 20 months after treatment; another had a deep cerebral tumour obstructing the foramen of Monro and was well 7 weeks later; while a third, who had multiple metastatic tumours, was improved for 7 months after an implantation which was limited to one of the tumour masses. The 2 other patients died, one having a teratomatous tumour into which haemorrhage occurred after operation and the other a cystic glioma, both tumours being situated in the cerebral hemispheres. The authors emphasize that all these patients were extremely ill at the time of treatment and that the improvement in the general condition of several of them was striking. They have demonstrated the postoperative reduction in the mass of the tumour by encephalography in 2 cases.

J. E. A. O'Connell

220. **Clinical and Pathological Aspects of Multiple Glioblastomata.** (Zur Klinik und Pathologie des multilokulären Glioblastoms)

H. TSCHABITSCHER and T. WANKO. *Wiener Zeitschrift für Nervenheilkunde* [*Wien. Z. Nervenheilk.*] **10**, 175–186, 1954. 6 figs., 19 refs.

The simultaneous appearance of several tumours of the central nervous system in one individual is a comparatively rare occurrence. In this paper from the University of Vienna the authors describe 3 cases in which tumours (glioblastomata) were found in more than one part of the brain. They discuss the difficulties in the diagnosis of such cases and examine the various

arguments as to whether these lesions are the result of metastases from one tumour or are tumours arising independently in several places at once. The former theory is thought to be the more likely.

G. S. Crockett

221. **The Clinical Aspects and Treatment of Cerebellar Astrocytoma.** (Zur Klinik und Therapie der Kleinhirnastrocytome)

K. HOLUB. *Wiener Zeitschrift für Nervenheilkunde* [*Wien. Z. Nervenheilk.*] **10**, 187–194, 1954. 8 refs.

The author reviews 54 cases of astrocytoma of the cerebellum seen at the First Surgical Clinic, University of Vienna, during the last 13 years, of which 33 showed cystic degeneration; the average age of the patients was 24. The main symptoms were nausea, vomiting, headache, and giddiness. In 44 cases there was papilloedema. The relatively good prognosis in this condition is stressed, one case being mentioned in which the patient survived for 45 years after the diagnosis without operation, while in other cases patients have been known to live for many years after only partial removal of the growth.

G. S. Crockett

222. **Hypothalamic Tumour. Correlation between Symptomatology, Regional Anatomy, and Neurosecretion**

A. B. ROTHBALLER and G. S. DUGGER. *Neurology* [*Neurology*] **5**, 160–177, March, 1955. 10 figs., bibliography.

223. **Treatment of Progressive Myoclonic Epilepsy with Mephenesin**

R. E. KELLY and D. R. LAURENCE. *British Medical Journal* [*Brit. med. J.*] **1**, 456–458, Feb. 19, 1955. 1 fig., 14 refs.

Myoclonic epilepsy is characterized both by its progressive nature and its intractability, the patients tending to relapse into status myoclonicus, becoming helpless and bedridden, and dying of exhaustion and inanition within 4 or 5 years of the onset. In one severely afflicted patient under treatment at St. Thomas's Hospital, London, the effects of an intravenous infusion of 1% mephenesin in normal saline proved strikingly successful in reducing the myoclonic jerks and in reducing or abolishing signs of epileptic activity in the electroencephalogram. Subsequent treatment with 2 g. of mephenesin (30 ml. of elixir) 4 times daily and 65 mg. of phenobarbitone three times daily controlled the condition quite well for 18 months, when cessation of treatment on account of vomiting resulted in a return of status myoclonicus. A further infusion of 1% mephenesin again proved successful and the patient is still (2 years later) " better than ever " while taking 1·25 to 2·5 g. of mephenesin carbamate 4 times daily and 65 mg. of phenobarbitone 3 times daily. In a second severe case the patient is also progressing well on a total daily dose of 30 g. of mephenesin, of which 8 to 10 g. is being taken as the elixir and 20 to 22 g. in the form of tablets. The authors also report the results in 3 other cases, in which, however, the duration of observation has been shorter, but already some improvement has been noted.

The site and mechanism of action of mephenesin, at present unknown, are discussed, and attention is drawn to the side-effects of the drug—dizziness, drowsiness, and vomiting. The elixir in large quantities is liable to induce drunkenness, since it contains 30% alcohol; it also acts as a local analgesic with undesirable results, and should therefore be taken preferably after meals. Mephenesin has been reported to cause haemolysis, but the authors have found no evidence of this when intravenous infusions were limited in strength to 1% solution in saline.

Fergus R. Ferguson

224. **Use of N-Methyl-α:α-methylphenylsuccinimide in Treatment of Petit Mal Epilepsy**

F. T. ZIMMERMAN and B. B. BURGEMEISTER. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat. (Chicago)*] **72**, 720–725, Dec., 1954. 4 refs.

A preliminary report is presented on a new anticonvulsant, N-methyl-α:α-methylphenylsuccinimide or " PM 396 ", which differs from " milontin " only by the introduction of a second methyl group.

In experiments carried out at Columbia University College of Physicians and Surgeons, New York, it was effective in protecting rats against " metrazol " (leptazol) convulsions in a dose of 65 mg. per kg. body weight (compared with 125 mg. of milontin per kg. and 500 mg. of trimethadione per kg.). The drug was administered to 54 patients with petit mal, none of whom had been controlled by previous medication: complete control was gained in 22%, " practical " control in 9%, and " partial " control in 29%. PM 396 was also of value in treating psychomotor seizures in a series of 15 patients, in 3 of whom the attacks were completely controlled, while 12 in all were benefited. Eleven patients (20%) in the former group showed some toxic symptoms, of which a drug rash was the most common.

Donald McDonald

225. **A Study of the Behaviour of Patients with Psychomotor Epilepsy in the Interval between Attacks.** (Étude du comportement des épileptiques psycho-moteurs dans l'intervalle de leurs crises)

H. GASTAUT, G. MORIN, and N. LESÈVRE. *Annales médico-psychologiques* [*Ann. med.-psychol.*] **1**, 1–27, Jan., 1955.

The authors describe investigations carried out on a group of 60 adults suffering from psychomotor epilepsy, the purpose being to study the social behaviour of these patients, who were aged between 20 and 50 and were of average intelligence. The methods included a clinical interview, evaluation of the results of psychological tests, and questioning of the patient's family. It was found that nearly all these patients showed disturbances in the fields of general activity and of social behaviour, and that they could be divided into two main psychological types.

The first type, which included more than two-thirds of the patients, was characterized by general psychomotor hypoactivity (bradyphrenia and bradykinesis), paroxysmal outbursts of unmotivated anger, and an electroencephalogram (EEG) suggestive of neuronal

hypoactivity. The second type, accounting for about one-quarter of the cases, was characterized by a normal or even slightly increased level of activity, permanent irritability without outbursts of violence, and an EEG suggestive of neuronal hyperactivity.

In the field of total activity, 72% of the patients showed on simple observation a sluggishness of ideation, speech, and gesture, which was expressed also in the psychometric tests. In 20% a contrasted syndrome of normal or hyperactivity was observed, and this also was reflected in the results of the psychometric and Rorschach tests. In the field of social behaviour 50% of the patients showed paroxysmal outbursts of anger, 25% permanent irritability without outbursts, and 7% had behaviour disturbances amounting to perversion. Only 8% of the patients showed no disturbance of activity or social behaviour or an abnormal EEG. The authors adduce experimental evidence indicating that psychomotor epileptics tend to behave like animals with chronic irritative lesions of the rhinencephalon. They suggest that the so-called "epileptic constitution" is identical with the personality type observed in the majority of these patients and that this constitution is found only in patients with disturbances involving the region of the diencephalon and rhinencephalon. Clinical evidence suggests that there is an interval of 4 to 6 years between the establishing of such a lesion and the appearance of personality changes. [The authors' reasons for regarding the paroxysmal outbursts as disorders of personality rather than as epileptic equivalents should be read in the original.] *J. B. Stanton*

226. **Mysoline. An Effective Anticonvulsant with Initial Problems of Adjustment**
W. H. Timberlake, J. A. Abbott, and R. S. Schwab. *New England Journal of Medicine* [*New Engl. J. Med.*] **252**, 304–307, Feb. 24, 1955. 13 refs.

227. **Surgical Alleviation of Parkinsonism: Effects of Occlusion of the Anterior Choroidal Artery**
I. S. Cooper. *Journal of the American Geriatrics Society* [*J. Amer. Geriat. Soc.*] **2**, 691–718, Nov., 1954. 22 figs., 21 refs.

The author describes his further experience, at the New York Hospital–Bellevue Medical Center, of surgical occlusion of the anterior choroidal artery in Parkinson's disease. Since the effect of occlusion of this artery on Parkinsonian tremor in the contralateral limbs was discovered accidentally by the author (*Surg. Gynec. Obstet.*, 1954, **99**, 207; *Abstracts of World Medicine*, 1955, **17**, 228) the operation has been deliberately performed on 34 patients. Resting tremor was virtually abolished in 70% [? 24] of these cases, rigidity was significantly reduced in every case in which occlusion was satisfactorily effected, and gait was improved—in some cases with disappearance of pro- and retro-pulsion. In only 5 cases was there loss of power following the operation, and the degree of incapacity was often markedly reduced—deformity disappearing in several cases even though of long standing. The average preoperative duration of symptoms was 15 years, and postoperative improvement has in some cases persisted for as long as 24 months. Although the occlusion has been performed bilaterally in 6 cases, the author advises that it should usually be confined to one side and limited to patients under the age of 55. The operative mortality was 10% [?4 deaths]. The anatomy of the anterior choroidal artery is described and an explanation for the benefits following its occlusion in Parkinsonism suggested.

[The main advantage of this procedure over other methods of surgical treatment in this disease lies in the fact that no loss of power follows the operation. If the early results are confirmed and the benefits persist it will prove a real advance in the treatment of severely disabled cases of Parkinsonism.] *J. E. A. O'Connell*

CRANIAL NERVES

228. **Alternating Contraction Anisocoria. A Pupillary Syndrome of the Anterior Midbrain**
O. Lowenstein. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat.* (*Chicago*)] **72**, 742–757, Dec., 1954. 9 figs., 9 refs.

Alternating contraction anisocoria is a condition in which stimulation of one eye by light results in greater constriction of the pupil of the stimulated eye than on the other side. If the phenomenon is restricted to one eye, stimulation of the other resulting in equal constriction of both pupils, it is described as unilateral; if it is caused by the stimulation of either eye it is described as bilateral. The author of this paper discusses the possible anatomical lesions responsible in great detail, and concludes that the condition is probably caused by a combination of lesions in the neurones of the first and second orders running to the Edinger-Westphal nucleus. The site of damage is thought to be in the posterior commissure and the brachia of the superior colliculus.

Among 690 subjects examined at the Presbyterian Hospital (Columbia University), New York, the syndrome was found 158 times (22·9%), being unilateral in 108 and bilateral in 50 cases. The syndrome occurred most commonly in association with infections of the central nervous system (35%); it was due to vascular lesions in 17%, to disseminated sclerosis in 11%, and to various degenerative conditions in 14%.

[It is not made clear whether the 690 subjects studied were neurological patients or selected at random from the hospital population, but the former seems more probable.] *Donald McDonald*

229. **"Epidemic Vertigo" with Oculomotor Complication**
A. W. D. Leishman. *Lancet* [*Lancet*] **1**, 228–230, Jan. 29, 1955. 5 refs.

The author describes 5 cases of "epidemic vertigo" all seen in consultant practice or at the Royal Infirmary, Sheffield, during the months of September and October, 1954. The first case—in a man of 54—there was sudden vertigo with paresis of the left superior rectus muscle, and the cerebrospinal fluid (C.S.F.) contained 8 lympho-

cytes per c.mm. and 70 mg. of protein per 100 ml. The patient improved slowly, but still had symptoms 14 weeks after the onset. The second patient seen, a girl of 19, had had no true vertigo, but tended to stagger to the right and suffered from drowsiness, headache, and vomiting; she recovered completely within 48 hours. The other 3 patients had typical vertigo, and 2 of them had transiently dilated, inactive pupils; the C.S.F. was quite normal in all 3.

All these patients were living in, or within a few miles of, the town of Rotherham, but so far as could be discovered no other case had occurred, nor were any seen in the adjacent city of Sheffield. It was impossible to trace any connexion between the 5 cases. Although he feels convinced that each of these patients had the same disease, the author does not feel justified in speculating on its nature.

[The abstracter prefers the more usual title of "labyrinthine neuronitis" for the condition exemplified by the last 3 cases. In the first case the abnormal C.S.F. suggests the possibility of disseminated sclerosis. In the second case there was no true vertigo and the condition was too transient to justify diagnosis. Five cases hardly make an epidemic.] *N. S. Alcock*

230. **Combined Trigeminal and Glossopharyngeal Neuralgia**

R. J. BRZUSTOWICZ. *Neurology* [*Neurology*] **5**, 1–10, Jan., 1955. 1 fig., 28 refs.

The author reviews 34 cases of glossopharyngeal neuralgia observed at the Mayo Clinic in the 15-year period 1935–50. He states that approximately 200 cases of trigeminal neuralgia are seen at the clinic each year, so that the ratio of cases of glossopharyngeal to trigeminal neuralgia is about 1:88.

Of the 34 patients, 9 (6 men and 3 women over the age of 40) had both trigeminal and glossopharyngeal neuralgia. The case histories of these are reported in detail.

The author states that in glossopharyngeal neuralgia the trigger zone is in the tonsillar fossa, and that the pain can be brought on by swallowing and can be relieved temporarily by cocaine. Discussing the possible anatomical basis for combined trigeminal and glossopharyngeal neuralgia he points out that the facial, glossopharyngeal, and vagus nerves contain somatic afferent fibres which end in the nucleus of the spinal tract of the trigeminal nerve. The age group of the affected patients in this series would suggest a vascular cause, but if this is central then such cases should be much more frequent than they are. A peripheral ischaemic mechanism is considered to be a more likely cause. In cases of combined trigeminal and glossopharyngeal neuralgia the operation of choice is Sjöqvist's trigeminal tractotomy, in which anaesthesia is produced in the entire somaesthetic system of the head on the side incised.

[The suggestion that a vascular disturbance is the cause of the neuralgia is still tentative; it is doubtful, therefore, whether it is profitable to discuss the site of this hypothetical lesion.] *N. S. Alcock*

SPINAL CORD

231. **The Early Diagnosis of Spinal Tumours**

H. J. G. BLOOM, H. ELLIS, and W. B. JENNETT. *British Medical Journal* [*Brit. med. J.*] **1**, 10–16, Jan. 1, 1955. 19 refs.

During the years 1940–51, 36 cases of spinal tumour were treated at the Military Hospital for Head Injuries at Oxford in 32 men and 4 women of ages ranging from 17 to 60 years. A number of these cases had been incorrectly diagnosed. Pain was the commonest symptom, and failure to recognize its type and distribution had most often led to wrong diagnosis. Eight of the patients had metastatic tumours with the short history and advanced signs characteristic of such cases. The commonest site of origin of these was the bronchial tree.

In 15 cases the tumour was classified as a neurofibroma, in none as a meningioma. Since in most civilian series these types occur in the ratio of 6 : 4, it will be readily seen that these cases, drawn from Service personnel, constitute a highly selected series. The importance of performing lumbar puncture to ascertain whether there is any degree of spinal block is emphasized. Radiology is discussed [but, as was pointed out in a subsequent letter by Bull (*Brit. J. med.*, 1955, **1**, 225), perhaps too little regard is given to the help which the radiologist today is able to give in deciding the nature and precise position of the tumour in relation to the cord and its coverings]. *Lambert Rogers*

232. **The Results of Intraspinal Injection of Hydrocortisone. A Preliminary Note.** (Premiers résultats sur l'emploi de l'hydrocortisone par voie intra-rachidienne. (Note préliminaire))

T. LUCHERINI. *Revue du rhumatisme et des maladies ostéo-articulaires* [*Rev. Rhum.*] **21**, 809–816, Dec., 1954.

The commonest cause of lumbar radiculitis is probably protrusion of a lumbar intravertebral disk, and since there is an accompanying inflammatory reaction it should be possible, the author argues, to influence the latter by means of intraspinal injection of hydrocortisone and thus reduce the usually prolonged period of invalidism. In 2 such cases seen at the Rheumatological Clinic, Rome, 25 mg. of hydrocortisone in normal saline was injected through the 4th intervertebral space; "spectacular" relief of spasm in the paravertebral muscles was obtained within 2 or 3 minutes, signs (for example, Lasègue's) and symptoms progressively diminished, and the cerebrospinal fluid remained unaffected. Thus encouraged, the author treated another 16 patients with lumbar radicular pain, the diagnosis being based on clinical and radiological findings. In a number of control cases the administration of cortisone systemically in doses of 100 to 150 mg. per day was without effect. In general, it was found that the more acute the onset, the more dramatic the result. In only 4 cases was a second injection required after mild recurrence of symptoms in 12 to 14 days. The electroencephalogram remained normal, but absent tendon reflexes did not return.

The author discusses the possible mode of action of the hormone, but admits that the intrathecal injection of 1 ml. of normal saline gives almost equally dramatic results; he suggests that Speransky's " spinal pumping " may explain this. *David Preiskel*

233. **Syringomyelia without Sensory Disturbance. The Diagnostic Value of Signs of Dysraphia.** (La siringomielia senza disturbi di senso. Valore diagnostico dei segni disrafici)
E. MANGHI. *Rassegna di studi psichiatrici* [*Rass. Studi psichiat.*] **43**, 883–895, 1954. 22 refs.

The author reports, from the Nervous Diseases Clinic, University of Parma, 3 cases of patients suffering from syringomyelia who were without the characteristic disturbances of sensation of temperature and pain. In all 3 there were signs in the lower limbs indicating lesions of upper motor neurones, such as hypertonus, paresis, and exaggeration of the tendon reflexes, but no sensory changes. In the upper limbs the symptoms were principally of weakness and wasting of the muscles of the forearm and hand, and in one case there was fibrillary fasciculation in these muscles. All 3 patients had abnormalities of the vertebral column of a developmental type, such as kyphosis or scoliosis or both, and in one there was also incomplete closure of the posterior sutures of the skull. This patient had been under observation for 14 years before the diagnosis of syringomyelia was eventually established by the development of the classic sensory dissociation in the upper extremities.

The author emphasizes that syringomyelia may be accompanied by developmental anomalies of the spinal column (status dysraphicus) and that syringomyelia should always be considered as a possible diagnosis in patients with such anomalies who develop neurological lesions referable to the cervical cord.

Donald McDonald

234. **The Syndrome of Herniation of the Lower Thoracic Intervertebral Discs with Nerve Root and Spinal Cord Compression. A Presentation of Four Cases with a Review of the Literature, Methods of Diagnosis and Treatment**
J. A. EPSTEIN. *Journal of Neurosurgery* [*J. Neurosurg.*] **11**, 525–538, Nov., 1954. 3 figs., 13 refs.

The case histories of 4 patients who were seen at St. John's Episcopal Hospital, Brooklyn, New York, with disabling symptoms caused by a herniated thoracic intervertebral disk are presented. Symptoms had been present for periods ranging from 4 months to 3 years and the patients had undergone numerous investigations, including unnecessary gynaecological operations on 2 of 3 women. In no case was trauma an aetiological factor. The main feature in the 3 female patients was incapacitating unilateral root pain of abrupt onset, and the author points out that such pain may closely mimic abdominal pain of visceral origin, intercostal neuralgia, angina, and other conditions and thus tend to mask the true diagnosis. Straining aggravated the pain in one case, and movements of the back precipitated it in 2. Neurological examination showed in 2 cases hyperalgesia and hyperaesthesia over the lower thoracic dermatomes, in the third case there was evidence of pyramidal-tract involvement, while the fourth patient (the only male) presented with a spastic ataxic gait of painless onset; sensory loss at the level of T 10 and urinary sphincter disturbance subsequently developed in this case. Radiography of the spine showed arthritic changes in only one case, and lumbar puncture yielded normal cerebrospinal fluid without any evidence of spinal blockage in all the cases. The diagnosis was established by myelography in each case, screening being the most valuable procedure; filling defects were observed at the T 11–12 interspace in 3 cases and at T 12–L 1 in the fourth.

Operation was performed in all cases, total laminectomy of at least two vertebrae being carried out in order to facilitate exposure. The dura was opened to permit examination of the cord before extradural removal of the protrusion with pituitary rongeurs, and marginal osteophytes were nibbled away. In the 3 cases with root pain the dorsal roots of the nerve involved were cut intradurally, producing postoperative relief from pain. Signs of cord compression were relieved completely in 2 cases and partially in the patient with a transverse lesion. In the author's experience the poor results which have often been reported after surgery can be avoided if the diagnosis is made before irreparable spinal cord injury has occurred. Detailed case histories are given and the literature is briefly reviewed.

J. V. Crawford

235. **The Treatment of Spastic Paraplegia by Selective Spinal Cordectomy**
C. S. MACCARTY. *Journal of Neurosurgery* [*J. Neurosurg.*] **11**, 539–545, Nov., 1954. 4 figs., 17 refs.

The author describes another method of producing flaccidity of the lower limbs in patients with spastic paraplegia due to irreparable spinal-cord damage, pointing out that spasticity produces so many difficulties in nursing, such as urological complications and bedsores, that only by producing flaccidity in the legs and bladder can these patients be adequately cared for. During recent years this has been achieved by means of anterior rhizotomy, subarachnoid injection of alcohol, or more rarely by posterior-column tractotomy. The additional procedure here described, which was developed by the author at the Mayo Clinic, is selective spinal chordectomy. Surgical excision of a portion or all of the malfunctioning part of the spinal cord is likened to removal of an atrophic cerebral hemisphere in patients suffering from infantile hemiplegia and uncontrolled convulsions. The selectivity of the procedure is stressed. In cases of injury to the cord in the upper thoracic region it is suggested that an isolated segment at the level of T 9 or 10 be left in place in order to maintain reflex abdominal tone in the hope of improving emptying of the bladder. In low thoracic-cord injuries, the lumbar and sacral portions of the cord can be accurately removed.

The first spinal chordectomy performed by the author, with Kiefer, was in 1948 (*Proc. Mayo Clin.*, 1949, **24**, 108; *Abstracts of World Surgery*, 1949, **6**, 90) for the

purpose of removing a glioma of the cord in a patient with spastic paraplegia. The present communication deals with 4 patients who sustained severe injury of the spinal cord with resultant paraplegia and spasticity. The management of these patients by removal of segments of the cord distal to the injuries is presented in detail. The procedure was reasonably successful in all 4 cases and good control of the bladder was achieved in 3. *J. V. Crawford*

236. **Cervical Myelopathy. A Common Neurological Disorder**

E. CLARKE. *Lancet* [*Lancet*] **1**, 171–176, Jan. 22, 1955. 2 figs., 43 refs.

Working at the Postgraduate Medical School of London, the author has studied 32 patients with cervical spondylosis, in all of whom clinical signs of spinal-cord disease were found. The patients are classified in four groups according to whether there were (1) symptoms in both upper and lower limbs, (2) symptoms of cervical-root irritation only, (3) neurological abnormalities without accompanying symptoms, or (4) signs of cervical myelopathy as a complicating factor in other diseases. The frequency of the condition is attested to by the fact that all these patients were seen during a period of 15 months in the wards or out-patient departments of a general hospital.

The diagnostic importance of reflex changes in the upper limbs, and particularly of inversion of the radial and biceps jerks, is stressed. The author also emphasizes the complete correlation between the results of manometry carried out with the neck in various positions and the myelographic findings. The problems of treatment are briefly reviewed: conservative handling, with a period of neck fixation combined with careful clinical observation and consideration of laminectomy should the disease continue to progress, is considered to be the most satisfactory approach. *E. C. Hutchinson*

DISSEMINATED SCLEROSIS

237. **Cerebral Metabolism of Glutamic Acid in Multiple Sclerosis**

J. E. ADAMS, H. A. HARPER, G. S. GORDAN, M. HUTCHIN, and R. C. BENTINCK. *Neurology* [*Neurology*] **5**, 100–107, Feb., 1955. 2 figs., 14 refs.

The authors, working at the U.S. Naval Hospital, Oakland, and at the University of California, San Francisco, have studied the cerebral metabolism of glutamic acid in 32 patients with disseminated sclerosis and in 19 control subjects of comparable average age, employing the Kety–Schmidt method. The subject was fasting and had received no medication for at least 24 hours. In an initial control study samples of arterial and mixed cerebral venous blood were drawn simultaneously at zero to 1 minute and at 3, 5, and 10 minutes while the subject breathed a mixture of 15% nitrous oxide, 21% oxygen, and 64% nitrogen. There was then an interval of 20 minutes for the expiration of the nitrous oxide, during which 20 ml. of a 30% solution of sodium succinate was injected slowly into an internal jugular vein, preceded by an intravenous injection of 0·5 mg. of atropine sulphate to prevent the fall in blood pressure which otherwise occurred. When the succinate had been given, blood samples were taken as before during inhalation of the nitrous oxide mixture. The glucose, lactate, oxygen, carbon dioxide, glutamic acid, glutamine, and (in some cases) pyruvic acid content of each blood sample was then estimated.

Before the administration of sodium succinate amidation of glutamic acid to glutamine was shown to occur in the brain in 15 of the 19 control subjects, but in only 5 of the 32 cases of disseminated sclerosis, this process being most severely impaired in patients showing clinical evidence of progression of the disease. In about half the patients, the defect was diminished or removed by the administration of sodium succinate. The authors suggest that the failure of amidation of glutamic acid in cases of disseminated sclerosis " may reflect a failure of one mechanism for elimination of ammonia from the brain ". *John N. Walton*

238. **Information Provided by Air Encephalography in Disseminated Sclerosis.** (Renseignements fournis par l'encéphalographie gazeuse au cours de la sclérose en plaques)

G. BOUDIN, J. BARBIZET, and —. MONGERMONT. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **31**, 15–18, Jan. 2, 1955. 5 figs., 9 refs.

Air encephalography and examination of the cerebrospinal fluid (C.S.F.) were carried out in 33 cases of disseminated sclerosis at the Salpêtrière Hospital, Paris. The C.S.F. findings in general confirmed those of earlier authors, 14 cases showing an increase in albumin content to 30 to 56 mg. per 100 ml., while globulin values proved inconstant. In 17 of 31 cases the colloidal benzoin test was abnormal, a moderate precipitation similar to that seen in neurosyphilis being observed; in 12 of these cases there was an increase in C.S.F. albumin content. In 10 the lumbar C.S.F. showed a lymphocytosis varying from 3 to 7 cells per c.mm., and in a further 3 cases 14, 16, and 38 cells per c.mm. respectively were present. C.S.F. withdrawn after the injection of 40 ml. of air was regarded as pericerebral in origin; in 17 of 31 of these cases there was a lymphocytosis of 13 to 104 cells per c.mm.

Pneumoencephalography showed dilatation of the lateral ventricles in 15 cases and slighter but definite changes, usually symmetrical, in a further 15. Commonly there was an excess of air over the hemispheres, particularly in the frontal region. The basal cisterns were not studied.

There was no relation between the changes in the C.S.F. and the radiological findings. The former are regarded as indicating an active process and are present in relapse, whereas the radiological changes seen were believed to be the result of scarring. There was no evidence that lumbar puncture aggravated disseminated sclerosis. *L. G. Kiloh*

See also Pathology, Abstract 10.

Psychiatry

239. **Curarization in Convulsion Therapy.** (La curarisation en convulsivothérapie)
J. BOUREAU. *Annales médico-psychologiques* [*Ann. méd.-psychol.*] **2**, 712–729, Dec., 1954. 2 figs.

A report is presented on the use of relaxants in the treatment by electric convulsion therapy (E.C.T.) of a series of 632 psychiatric patients, who received a total of 4,055 shocks. Of the patients, 25% were under 40 years old, 66% between 40 and 60, 27% between 60 and 70, 8% between 70 and 80, and 1% over 80. The oldest was 92 years old. Objective measurements of the degree of muscular contraction occurring under E.C.T. with and without modification were made by means of the electromyograph and of an apparatus similar to the hysterotonometer, which recorded changes in the volume of the calf muscles during contraction.

The intensity both of the initial generalized contraction and of those of the tonic and clonic phases was reduced by tubocurarine in doses of 10 to 32 mg., by " flaxedil " (gallamine) in doses of 40 to 100 mg., and particularly by succinylcholine in doses of 15 to 100 mg., this last drug being preferred by the author. It has the double advantage over tubocurarine and gallamine that the relaxation produced is greater and lasts for a shorter time, so that the risks are greatly reduced.

The author recommends that succinylcholine be given intravenously after the injection of thiopentone, using the same needle, since when the two are given simultaneously curarization develops before narcosis. Oxygen is given before as well as after the shock, this being considered the best safeguard against cardiovascular accidents. The author's series included 14 patients who were treated successfully in spite of previous coronary thrombosis, and it is emphasized that the administration of oxygen before the shock is essential in such cases owing to their enhanced sensitivity to anoxia. The same holds good for asthmatics, who have the further disadvantage of being sensitive to barbiturates, and the use of " phenergan " (promethazine) and larger doses of atropine are recommended in addition in allergic subjects. Only 3 fatal accidents are reported—2 due to asphyxia and faulty resuscitation and one to cardiac syncope—among the 4,055 treatments given. All occurred before the use of succinylcholine and oxygenation treatment were adopted.

The author concludes that by the use of muscle relaxants the benefits of E.C.T. may be extended to patients hitherto barred from them by old age or physical illness, and that these drugs are very safe in experienced hands.

Richard de Alarcón

240. **Fatal Agranulocytosis during Treatment with Chlorpromazine**
J. R. TASKER. *British Medical Journal* [*Brit. med. J.*] **1**, 950–951, April 16, 1955. 4 refs.

241. **Chlorpromazine as a Therapeutic Agent in Clinical Medicine**
J. H. MOYER, V. KINROSS-WRIGHT, and R. M. FINNEY. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 202–218, Feb., 1955. 2 figs., 15 refs.

242. **Post-puerperal Recurrent Depression**
A. B. HEGARTY. *British Medical Journal* [*Brit. med. J.*] **1**, 637–640, March 12, 1955. 4 refs.

The author describes 7 cases, observed for periods varying from 3 months to 2 years, in which recurrent depression was related to the menstrual cycle, the condition usually becoming worse premenstrually. The illness started in each case with puerperal depression from which the patient never completely recovered, the age of onset being 22 in one case and averaging 32 in the remaining 6. All 7 were of pyknic build and moderately obese. Most of them had previously shown some mild cyclothymic traits of personality, but all had been happy and well adjusted. One patient had a history of a previous non-puerperal depressive attack. Six of the patients gave a history of emotional stress in the puerperium, with an infective illness in 2 cases. A second childbirth aggravated symptoms in 2 cases.

The symptoms of the illness, which was having a disturbing and disintegrating effect on family life, consisted in depression and irritability, obsessive fears, impulses to harm the child or commit suicide, fatiguability, and sometimes menopausal symptoms such as flushing and palpitations, menstrual irregularities, and oligomenorrhoea. The severity of these symptoms varied considerably from case to case, and there were periods of freedom from symptoms ranging from a few days to 3 months. The possibility of spontaneous recovery after the menopause is suggested by the apparent absence of similar cases in post-menopausal women, but in the absence of knowledge of the nature of the depressive state and of the neuro-endocrinological effects of puerperal and premenstrual involutionary processes no conclusion can be reached concerning the aetiology of this relatively common condition. The importance of differentiating cases of this type from cases of psychoneurosis and involutional depression is stressed—in the condition described the history and previous personality are quite different, and the short periodicity of attacks is characteristic.

Treatment with dexamphetamine (5 to 10 mg.) and amylobarbitone (65 mg.) twice daily was beneficial in all cases, the response being dramatic in 4. In all but one case, however, withdrawal of the drugs led to a relapse, and treatment had to be resumed. Other forms of treatment, including electric convulsion therapy, acetylcholine shock, administration of various hormones, and psychoanalysis, were tried without success.

Elizabeth M. Watkins

Dermatology

243. **Investigations into the Effect of Autohemotherapy.** [In English]
V. A. FRANDSEN and T. SAMSØE-JENSEN. *Acta allergologica* [*Acta allerg. (Kbh.)*] **8**, 26–30, 1955. 16 refs.

The clinical effects of certain forms of non-specific protein therapy used in allergy and dermatology have been attributed in part to stimulation of the adrenal cortex. In an investigation carried out at Rigshospitalet, Copenhagen, no evidence of adrenocortical stimulation in the form of eosinopenia or increased excretion of 17-ketosteroids could be found in 16 patients with various skin diseases who received autohaemotherapy, 10 ml. of their own blood being injected intramuscularly on 3 consecutive days. *A. W. Frankland*

244. **The Effectiveness of Hydrocortisone Ointment in Various Cutaneous Diseases. A Continued Study**
B. HEILESEN, A. KRISTJANSEN, and F. REYMANN. *Dánish Medical Bulletin* [*Dan. med. Bull.*] **1**, 171–175, Nov., 1954. 11 refs.

The authors report, from the Rudolph Bergh Hospital, Copenhagen, the long-term results of prolonged treatment with hydrocortisone ointment in a variety of skin diseases such as anal pruritus, ano-genital eczema, neurodermatitis, and other lesions which often subside when the external stimuli of itching and scratching are removed for some length of time. The ointment employed contained essentially 100 mg. of hydrocortisone per 5 g. of base.

The results of therapy in each type of lesion are described in detail; definite improvement was noted in 29 out of 43 cases of ano-genital eczema, 25 of 30 cases of neurodermatitis, 49 out of 71 of atopic dermatitis, 53 out of 70 of eczema, and in 13 out of 20 cases of pityriasis simplex eczematisata. The authors conclude that although hydrocortisone ointment does not effect a cure, it may do much to alter the social destiny of many of these patients. They regard it as a valuable new addition to the methods of treatment of these types of lesion, but suggest that it be employed only for patients who have derived no benefit from conventional therapy. *G. B. Mitchell-Heggs*

245. **The Adrenal Cortex in Dermatomyositis.** (Die Beziehung der Dermatomyositis zur Nebennierenrinde)
M. MÜLLER. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **130**, 1287–1293, 1954. 22 refs.

The cause of dermatomyositis is unknown; the disorder commonly follows such diverse conditions as infection, trauma, or neoplasm. The striking muscular dysfunction is thought to be a result of disturbed mineral metabolism, in particular a lack of potassium. Potassium is necessary both for the contraction and relaxation of muscle fibres, and its level in the blood is under adrenocortical control. The excess of urinary creatinine which is found in dermatomyositis and which is due to failure to resynthetize phosphagen can be abolished by giving corticoids. Therapeutic trials with ACTH and cortisone have repeatedly shown that both the local and general abnormal mineral metabolism returns to normal while the hormone is being administered.

In the series of cases of dermatomyositis here reported from the Municipal Skin Clinic, Dresden, the level of urinary 17-ketosteroids was found to be markedly diminished, the Thorn test and estimation of serum electrolyte and uric acid levels and of urinary creatinine excretion all returning values strongly suggestive of adrenocortical deficiency [unfortunately direct estimation of urinary corticosteroid excretion was not carried out]. The author concludes that dermatomyositis is the result of constitutional or acquired pituitary–adrenal insufficiency, combined with some exogenous noxious factor such as trauma, infection, or neoplasm. The paper contains numerous references to the literature.
G. W. Csonka

246. **Sézary's Syndrome**
W. E. ALDERSON, G. I. BARROW, and R. L. TURNER. *British Medical Journal* [*Brit. med. J.*] **1**, 256–260, Jan. 29, 1955. 5 figs., 16 refs.

From the Royal Infirmary and St. Luke's Hospital, Bradford, 2 further cases of Sézary's syndrome are reported, to be added to the 5 confirmed cases previously recorded in the literature. The clinical and pathological aspects of the authors' 2 cases are described in detail and illustrated with photographs and photomicrographs. The features of this chronic condition, which usually attacks elderly females, are intense pruritus, generalized erythrodermia, pigmentation, and superficial lymphadenopathy associated with the presence of unusual monocytoid cells in the blood. These, termed " Sézary cells ", are approximately twice the size of normal polymorphonuclear granulocytes; their scanty, feebly basophilic cytoplasm resembles that of normal monocytes and contains fine granules or pseudopodia; the nucleus occupies about four-fifths of the cell and varies considerably in shape, while nucleoli are usually absent or indistinct. There may also be patchy loss of hair, dystrophy of the nails, arthropathy, and excoriations. In both the cases reported by the present authors the condition was relieved by the administration of cortisone or ACTH (corticotrophin), but relapsed on withdrawal of the drug.

The differential diagnosis from lipomelanic reticulosis, Hodgkin's disease, the leukaemias, and mycosis fungoides is discussed and the relation of the syndrome to the reticuloses is considered. The authors conclude that Sézary's syndrome is probably a local reticulosis intermediate between a benign reaction, such as lipomelanic reticulosis, and frank malignancy, as in reticulum-cell reticulosis. They suggest that the chronicity of the

disease is partly due to its premalignant character and partly to the organs affected—the skin and superficial lymph nodes. *Benjamin Schwartz*

247. **Chloroquine Sulphate in Treatment of Chronic Discoid Lupus Erythematosus**
H. J. LEWIS. *British Medical Journal* [*Brit. med. J.*] **1**, 329–330, Feb. 5, 1955. 4 refs.

248. **Aetiology of Dermatitis Herpetiformis and Pemphigus Chronicus.** [In English]
M. MELCZER. *Acta medica Academia Scientiarum Hungaricae* [*Acta med. Acad. Sci. hung.*] **6**, 255–272, 1954. 20 figs., bibliography.

From the University Medical School, Pécs, Hungary, the author presents experimental evidence which seems to support the view that dermatitis herpetiformis and chronic pemphigus are of viral origin, and claims to have successfully transmitted the causal organism by inoculation of chick embryos with filtrates of vesicle fluid or bacteriologically sterile cerebrospinal fluid obtained by lumbar puncture. He therefore suggests that these diseases are chronic, viral, non-epidemic diseases of the central nervous system which are accompanied by skin symptoms. *E. W. Prosser Thomas*

249. **Skin Reactions beneath Adhesive Plasters**
B. RUSSELL and N. A. THORNE. *Lancet* [*Lancet*] **1**, 67–70, Jan. 8, 1955. 3 figs., 11 refs.

Although adhesive plasters have been widely used for many years, comparatively few clinical investigations of the skin reactions beneath such plasters have been undertaken. In this paper from the London Hospital the authors describe 5 types of reaction due respectively to: (1) trauma of removal of the plaster; (2) irritation by the adhesive; (3) retention of sweat and serous discharges; (4) disturbance of the bacterial flora; and (5) sensitization.

(1) The traumatic reaction of removal occurs mostly at pilosebaceous orifices and is seen as follicular papules with some diffuse or blotchy erythema. It is observed a few minutes after the plaster is removed, particularly at hairy sites and when no solvent is used to aid removal. It is most marked with "tacky" plasters. (2) Irritation gives rise to red papules and pustules, with erythema but without vesiculation; these are more pronounced on moist skin and after prolonged application of the plaster. The keratoplastic properties of certain chemicals in some adhesive materials, particularly coal-tar derivatives, may be a cause of the irritation. There are fewer rashes when plaster free from rubber and resins is used, but such plaster is only "semi-adhesive". (3) Reactions due to retention of sweat and serous discharge beneath the plaster lead to maceration of the horny layer of the skin, infection, or infective eczema. There is no significant difference in the incidence of rashes when plaster containing fatty acids is used. (4) The addition to the adhesive plaster of an antiseptic with disparity of action against different organisms may predispose to bacterial infection from surviving organisms. (5) Reactions due to sensitization are not so common as reactions from irritation. They develop after a latent period of days with the first exposure or after a few hours with subsequent exposures, and are characterized by erythema, oedema, and vesiculation. The constituents of plasters which are most likely to cause such reactions include colophony resin, crêpe rubber, smoked rubber, rubber antioxidants, plasticizers, and antiseptics. Wool fat (lanolin) is an occasional sensitizer. In the authors' view these reactions could be avoided by using deproteinized rubber, abandoning the use of chloroxylenol, and substituting for colophony some other resin of lower sensitizing potential. *Kate Maunsell*

250. **Cutaneous Side-effects of Largactil.** (Zur Kenntnis der Largactil-Nebenwirkungen an der Haut)
T. KRAJEWSKI. *Zeitschrift für Haut- und Geschlechtskrankheiten* [*Z. Haut- u. GeschlKr.*] **18**, 44–46, Jan. 15, 1955. 5 refs.

The author reports that among the patients and medical and nursing staff of a neurological clinic, 19 developed sensitization of the skin after contact with "largactil" (chlorpromazine hydrochloride). Local treatment with antihistaminics was unsuccessful and the skin lesions cleared only when administration or skin contact with the drug was completely stopped. In a few of the patients the skin lesions developed acutely within 10 minutes' exposure to sunlight, suggesting a photosensitive action. A number of those affected gave a history of an allergic diathesis, and it is suggested that such persons should in future be excluded from coming in contact with the drug. The author also suggests that the duties of the nursing staff should be arranged in such a way as to prevent the handling of largactil for more than 4 weeks at a time. *G. W. Csonka*

251. **Tuberculous and Tuberculoid Complications during Treatment of Lupus Vulgaris with Calciferol**
P. V. MARCUSSEN. *Danish Medical Bulletin* [*Dan. med. Bull.*] **1**, 165–171, Nov., 1954. 2 figs., 45 refs.

The author has investigated, at the Finsen Institute, Copenhagen, the incidence of tuberculous and tuberculoid complications arising during the treatment with calciferol of 284 patients suffering from lupus vulgaris. The technique employed, the ancillary pathological investigations undertaken over a prolonged period, and the various dermal and pulmonary complications (mainly benign) which arose are described. It is suggested that the majority of these complications arise as a direct consequence of treatment, presenting a picture corresponding to the haematogenous spread of tubercle bacilli; this, it is thought, may result from the fact that calciferol has an inhibitory or destructive influence on lupus tissue without affecting the virulence of the bacillus. It is emphasized that calciferol treatment of lupus vulgaris without simultaneous chemotherapy or local treatment with antibiotics may involve a greater risk than has been previously realized. *G. B. Mitchell-Heggs*

252. **The Onychodermal Band in Health and Disease**
R. B. TERRY. *Lancet* [*Lancet*] **1**, 179–181, Jan. 22, 1955. 2 refs.

Paediatrics

NEONATAL DISORDERS AND PREMATURITY

253. **Control of Cross-infection by Means of an Antiseptic Hand Cream**
J. MURRAY and R. M. CALMAN. *British Medical Journal* [*Brit. med. J.*] **1**, 81–83, Jan. 8, 1955. 7 refs.

The organisms encountered most frequently in cross-infection in hospitals are pyogenic staphylococci and streptococci, the former being responsible for much minor infection in the newborn. At Queen Charlotte's Maternity Hospital, London, 60% of the nurses were found to be nasal carriers of pyogenic staphylococci, and the hands an easy vehicle for transference of the organisms. The authors therefore investigated the efficacy of a hand cream ("hibitane"), in which is incorporated 1% of 1:6-di-4′-chlorophenyldiguanidohexane (" 10,040 "), in controlling cross-infection.

Among various laboratory tests carried out was the " finger-tip contamination test ". In this, 0·2 g. of the cream was rubbed well into the fingers and after 30 minutes and again at one hour the fingers were pressed for 30 seconds on to filter-paper moistened with a culture of *Escherichia coli*. After the fingers had been allowed to dry in air for one minute they were then pressed on to horse-blood–agar plates for 30 seconds and the number of resulting colonies of the organism counted at 24 and 48 hours. There was found to be a notable reduction in the number of bacteria which were transferred by the treated fingers as compared with control untreated fingers. The results of this and some other tests are presented in tables.

The antiseptic cream was then made generally available to the hospital staff, 1·5 to 2 g. to be rubbed on the hands after washing. This practice has now been in use at the hospital for some 18 months and no serious cases of staphylococcal infections have occurred, while any which have occurred were sporadic, and not in groups in certain wards as previously. *Elaine M. Osborne*

254. **Clinical Observations on the Prophylaxis of Ophthalmia Neonatorum**
I. MANN. *British Journal of Ophthalmology* [*Brit. J. Ophthal.*] **38**, 734–741, Dec., 1954. 1 fig.

The author suggests that the time has come for a revaluation of the well-tried prophylactic measure, introduced by Crédé, of treating the eyes of newborn infants with silver nitrate solution. She therefore undertook a clinical experiment at the King Edward Memorial Maternity Hospital, Perth, Western Australia, where this has been the routine practice since the hospital was founded. In this area gonorrhoea is uncommon, but penicillin-resistant strains of staphylococci are prevalent. The trial was carried out on 1,148 infants, who were divided into two groups of 569 and 579 respectively and observed for the first 12 days of life; in Group 1 the eyelids were cleansed at birth with normal saline solution, in Group 2 one drop of 1% solution of silver nitrate was instilled in addition.

Any " stickiness " about the eyes was recorded as discharge. This was noted in 100 cases in Group 1 (control group) and in 72 in Group 2; a higher proportion of these cases appeared within the first 4 days in Group 2 than in Group 1, but the former also had a higher proportion of negative cultures. The author suggests that possibly at this stage the discharge without infection was attributable to the reaction to silver nitrate. Over the whole observation period potential pathogens were isolated from 17·5% of Group 1 and from 12·4% of Group 2, the organisms found being *Staphylococcus albus* (both haemolytic and non-haemolytic), *Staph. aureus* (haemolytic, coagulase positive and negative), *Streptococcus viridans* (1 case), and *Escherichia coli* (1 case). There were 4 fairly severe cases of conjunctivitis in Group 1, but none in Group 2, although bacteriologically some of the infections in the latter were potentially worse and included 8 cases of double infection. The fact that no serious infection actually developed in Group 2 may be considered evidence of local resistance in those treated with silver nitrate. In neither group was there any case of severe purulent ophthalmia, and all the infants were discharged from hospital with clean eyes.

Sensitivity to antibiotics and chemotherapeutic agents was tested in a certain number of cases. Streptomycin alone gave a universally positive result, no organism showing resistance to this antibiotic; aureomycin came next, followed by chloramphenicol; penicillin and sulphadiazine were apparently of little value. Clinically, the use of antibiotics is usually unnecessary, but streptomycin would be the antibiotic of choice. The majority of infections in both groups cleared up with frequent saline swabbing, clearance in Group 2 being achieved more quickly. The author concludes that the use of silver nitrate reduces the incidence of infection, as distinct from discharge, in the first 12 days of life, but that its use is unnecessary in an efficient hospital in a country where the incidence of gonorrhoea is low, but " should still be considered as desirable in primitive conditions among infected populations ". *V. Reade*

255. **Retrolental Fibroplasia and Interstitial Pneumonia.** (Retrolentale fibroplasie en interstitiële pneumonie)
W. A. MANSCHOT and M. STRAUG. *Nederlandsch tijdschrift voor geneeskunde* [*Ned. T. Geneesk.*] **99**, 92–97 Jan. 8, 1955. 6 figs., 16 refs.

Post-mortem examination at the Municipal Hospital, Rotterdam, of the eyes of 59 premature infants who had had no ophthalmological investigation during life revealed 3 cases in which there was evidence of the earliest stage of retrolental fibroplasia, namely, oedema and increase of the capillary-forming mesenchymal cells

in the layer of nerve fibres, with penetration of the membrana limitans interna and formation of preretinal plexuses. The clinical records showed that all 3 infants had received oxygen and penicillin, and in the period preceding death had shown signs of dyspnoea, cyanosis, and severe anaemia. Examination of the lungs at necropsy revealed in all 3 cases the presence of subchronic interstitial pneumonia, which the authors interpret as an advanced stage of interstitial plasma-cell pneumonia; no trace of the causal organism *Pneumocystis carinii* was found, however. It is noted that interstitial plasma-cell pneumonia occurs almost exclusively in premature infants and particularly in those whose birth-weight is below 1,500 g., which is also of course the group in which retrolental fibroplasia is most likely to be found.

These two conditions, which are both of comparatively recent recognition, are connected, and the authors cite the observation of Ashton *et al.* (*Brit. J. Ophthal.*, 1953, 37, 513)—that hyperoxia produces an irreversible closure of the developing retinal arteries—to show the superficial nature of the apparent connexion between the increased use of oxygen for premature infants and the post-war increase in the incidence of retrolental fibroplasia. They point out that when the infant is restored to a normal atmosphere the resultant retinal ischaemia leads to the increased production of retinal capillaries; the sequence is therefore: interstitial plasma-cell pneumonia—administration of oxygen—retinal hypoxia—retrolental fibroplasia. In addition, high concentrations of oxygen in the lungs and the administration of penicillin may favour the multiplication of *Pneumocystis carinii*. They conclude by suggesting that the connexion between these two conditions may thus serve to explain the apparent epidemic occurrence of retrolental fibroplasia.

R. Crawford

256. **Epidemiology of Retrolental Fibroplasia. Its Etiologic Relation to Pulmonary Hyaline Membrane**
T. H. INGALLS. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 1017–1022, Dec. 16, 1954. 5 figs., 23 refs.

257. **The Bilirubin Content of Cord-blood Serum and the Blood Group of Mother and Child.** (Bilirubin im Nabelschnurserum und Blutgruppen bei Mutter und Kind)
H. CZERMAK and H. G. WOLF. *Helvetica paediatrica acta* [*Helv. paediat. Acta*] 9, 476–481, 1954. 9 refs.

The authors, working at the University Paediatric Clinic, Vienna, have attempted to answer four questions. (1) Is there any relationship between the cord-blood bilirubin level and the blood groups of mother and child? (2) What is the maximum figure for cord-blood bilirubin content? (3) Do premature infants show higher values than full-term ones? (4) Is there any relationship between cord-blood bilirubin content and the intensity and duration of physiological jaundice?

From a study of the 280 reliable results obtained out of 500 cases in which the cord-blood bilirubin content was determined, using the method described by Malloy and Evelyn, the authors conclude that the answers to these four questions are as follows. (1) There is no relationship between the cord-blood bilirubin value and the blood groups of mother and child. (2) The highest value for bilirubin obtained in this study was 2·9 mg. per 100 ml. of cord blood. (3) There is no difference between the bilirubin levels in the cord blood of premature and full-term infants. (4) The bilirubin content of the cord blood is no guide to the duration or intensity of the ensuing physiological jaundice.

J. G. Jamieson

258. **Exchange Transfusion as a Means of Removing Bilirubin in Haemolytic Disease of the Newborn**
G. H. LATHE. *British Medical Journal* [*Brit. med. J.*] 1, 192–196, Jan. 22, 1955. 5 figs., 20 refs.

Brain damage associated with a great excess of bilirubin in the plasma occurs in (1) haemolytic disease of the newborn due to iso-immunization to the blood-group antigens D, E, A, and S, (2) in certain premature babies without haemolytic disease, and (3) in some types of familial hyperbilirubinaemia. In the first two conditions the yellow pigment present in the affected brain has been shown to be the indirect-reacting bile pigment of the plasma, bilirubin. Since there is strong evidence that bilirubin is directly toxic to brain tissue, treatment in haemolytic disease of the newborn should be directed towards preventing an undue rise in the plasma bilirubin level, and the present author, working at Queen Charlotte's Maternity Hospital, London, has explored the possibility of achieving this aim by means of exchange transfusion.

Studies of the changes in the concentration of bile pigments in the plasma in cases of haemolytic disease and during the course of exchange transfusions showed that an exchange of 50 to 60 ml. of blood per lb. (110 to 132 ml. per kg.) body weight could be expected to lower the plasma bile-pigment concentration by 30 to 50%. At the same time it was observed that the amount of bile pigment removed by a large exchange was always greater than the amount that the baby's blood had been calculated to contain, and that the reduction in the plasma pigment level was less than that to be expected from the exchange of blood alone. These disparities can be explained only by assuming that pigment passes from the tissues into the circulation during the transfusion. Thus reduction of the plasma bilirubin level by exchange transfusion has the effect of washing excess bile pigment out of the tissues, but it is emphasized that such treatment will not prevent the level from rising again so long as the capacity of the liver to remove bilirubin remains inadequate. The author also points out that unless recently drawn blood is used for exchange, bile pigment derived from the breakdown of transfused erythrocytes may add considerably to the baby's load. The excretory capacity of the liver being very greatly reduced in premature infants, they are liable to develop brain pigmentation whether suffering from haemolytic disease or not. The period of danger in any case lasts for only 36 to 48 hours, but any rise in the plasma bilirubin concentration above the critical level during this time may cause serious damage. In a series of cases

reported by Mollison and Cutbush it was found that a level of 19 to 24 mg. of bilirubin per 100 ml. of plasma caused brain damage in 1 of 13 infants, the proportion increasing to 4 out of 12 at 24 to 29 mg. per 100 ml., while above this level the majority of infants were affected. The author suggests that exchange transfusion should be performed whenever the plasma bilirubin level reaches 20 mg. per 100 ml., being repeated as necessary until the excretory capacity of the liver becomes adequate.

A number of cases are reported in detail to illustrate the changes in the content of haemoglobin and total bile pigment in the blood of normal and affected babies and the need for treatment to be instituted before the plasma bilirubin level has risen to a dangerous height. In addition, a case of " inspissated bile syndrome " is described to show the confusion which may be caused by this factor. After an immediate exchange transfusion at birth the bile-pigment level in this patient's plasma increased rapidly. A second exchange transfusion was given at 48 hours, followed by a third at 75 hours. It was then found that of the 24 mg. of pigment per 100 ml. of plasma only 5·3 mg. was bilirubin, the rest being direct-reacting pigment, the toxic effect of which on brain tissue is still uncertain. *A. White Franklin*

259. **Icterus Gravis and Kernicterus in Premature Infants without Demonstrable ABO or Rhesus Incompatibility.** (Über den Icterus gravis und Kernicterus bei Frühgeburten ohne nachweislichen ABO- und Rhesus-Blutgruppen-antagonismus)
J. C. W. BAKKER. *Acta paediatrica* [*Acta paediat. (Uppsala)*] **43**, 529–542, Nov., 1954. 3 figs., 46 refs.

Of a group of 172 healthy premature infants cared for at the Hospital of St. John of God, The Hague, in tents in which a concentration of about 60% oxygen was maintained, 56 developed icterus gravis and 33 kernicterus. Of the latter, 21 died and in 14 cases in which necropsy was performed the diagnosis was confirmed. In none of these cases could any blood incompatibility be demonstrated between mother and child. In a comparable group of 139 premature babies given no oxygen therapy, icterus gravis without blood incompatibility occurred in 7 cases and kernicterus in one.

In the absence of blood incompatibility to account for the complications, the author discusses the possibility that the sudden change in oxygen tension between intra- and extra-uterine life may result in rapid destruction of erythrocytes and a consequent release of excess bilirubin, which cannot be adequately dealt with by the immature liver. Indeed in this group of infants the bilirubin level in the cerebrospinal fluid reached a mean of 2·5 mg. per 100 ml. and in the serum of 46·5 mg. per 100 ml. The author's view was confirmed by placing other premature infants, who were aged about one month old, but still several weeks premature, in a similar concentration of oxygen for about 10 days, when the haemoglobin level and erythrocyte count, which had previously been stabilized, fell by 27 to 30% during oxygen treatment, but began to rise immediately the infants were returned to a normal atmosphere. As a result of this experience the author advocates the limited use and careful control of oxygen therapy for premature infants.

Mary D. Smith

260. **Hypothermia in the Premature Infant.** (Unterkühlung bei Frühgeborenen)
G. JOPPICH and H. SCHÄFER. *Deutsche medizinische Wochenschrift* [*Dtsch. med. Wschr.*] **80**, 73–75, Jan. 14, 1955. 4 figs., 9 refs.

The reasons for the grossly subnormal temperature not infrequently found in premature babies on admission to hospital are discussed, and it is pointed out that the mortality among these infants is generally higher than the average for premature infants. It is the usual practice in such cases to take steps to raise the baby's temperature to normal as fast as possible, but in view of the beneficial effects on premature infants of artificially-induced hypothermia (" artificial hibernation "), as reported by French authors, it seemed possible that such rapid warming might contribute to the high mortality. No attempt was therefore made, in the treatment of a series of 45 premature babies admitted to the Children's Clinic of Göttingen University with a temperature below 36° C. (96·8° F.), to raise this to the normal level by special measures. There were 7 deaths (15·5%), all but one in infants of less than 1,500 g. birth weight, compared with a mortality among all premature infants treated during the same period of 30%.

I. A. B. Cathie

CLINICAL PAEDIATRICS

261. **Congenital Malformations of the Cardiovascular System in a Series of 6,053 Infants**
M. R. RICHARDS, K. K. MERRITT, M. H. SAMUELS, and A. G. LANGMANN. *Pediatrics* [*Pediatrics*] **15**, 12–29, Jan., 1955. 45 refs.

In an investigation into the effect on the outcome of pregnancy of infections and other complications during it, carried out at the Columbia–Presbyterian Medical Center, New York, 6,053 live or stillborn infants resulting from 5,964 pregnancies were examined. The examination of liveborn infants, which included routine radiography of the chest with additional investigations in those cases in which cardiovascular disease was suspected, was carried out at birth and repeated at 6 months and at 12 months.

Among the 6,053 infants, 50 (0·83%) were found to have congenital defects of the cardiovascular system. Omitting the 314 infants who weighed less than 500 g. at birth, the incidence of such defects among the 111 stillborn infants was 5·4%, while among the 98 who died within the first month it was 10·2% and among the remaining 5,530 infants 0·6%. (When further corrected by the omission of all cases in which necropsy was not performed or in which observation was not continued for the full 12 months these figures become 6·3%, 10·9%, and 0·6% respectively.) The incidence among premature liveborn children was 1·73%, as opposed to 0·49% among full-term babies. Congenital defects of the heart appeared to be most common in third pregnancies,

and their incidence rose with maternal age. On the other hand the incidence did not seem to be related to the sex or colour of the infant, or to the occurrence of acute or chronic infections or other conditions, vaginal bleeding, toxaemia, or pelvic tumours in the mother during pregnancy. The incidence of previous abortions or stillbirths was no greater amongst the mothers of affected children than of those unaffected, and the season of conception appeared to have no influence.

The type of defect was diagnosed definitely in 27 cases (25 at necropsy, 2 on strong clinical grounds), and provisionally in 23, the distribution being as follows:

Type of defect	Definite Diagnosis	Provisional Diagnosis
Fallot's tetralogy	5	3
Patent ductus arteriosus ..	5	—
Anomalies of great vessels ..	9	—
Septal defects	2	16
Others	6	4
Total ..	27	23

Of the 43 liveborn infants suffering from congenital heart defects, 16 (37·2%) died in the first 2 years of life, death being attributed to the cardiac defect in 12 (27·9%) of these. Of the 50 infants affected, 18 (36%) had other congenital abnormalities, mongolism (4 cases) being the commonest, followed by cataract, cleft palate, and diaphragmatic hernia (3 cases each).

[This paper is of interest so far as the analysis of the possible aetiological factors is concerned. But as the authors point out, the real incidence of congenital cardiac defects in this series may be higher than the figures given, which relate only to those cases in which signs or symptoms developed during the first year. Moreover, the provisional diagnoses made are clearly unreliable, as neither cardiac catheterization nor cardio-angiography was used, and this may account in part for the differences in incidence of the various abnormalities between this and most other series reported in the literature.] *H. G. Farquhar*

262. **Evaluation of the Flush Technique for the Determination of Blood Pressure in Infancy**
M. P. SULLIVAN and M. KOBAYASHI. *Pediatrics* [*Pediatrics*] **15**, 84–87, Jan., 1955. 5 refs.

The authors estimated the systolic blood pressure of 160 infants 8 to 11 months old by the " flush " technique described by Goldring and Wohltmann (*J. Pediat.*, 1952, **40**, 285). The procedure employed consisted in applying a bandage around the foot or hand sufficiently tightly to cause blanching. A 4·5-cm. sphygmomanometer cuff applied around the proximal half of the limb was then inflated to a pressure of 140 mm. Hg, the bandage removed, and the pressure lowered at a rate not faster than 7 mm. Hg per second, the point at which flushing of the sole of the foot or the palm of the hand occurred being taken as the systolic pressure. In each case 3 readings were taken on the right arm and three on the right leg.

For purposes of analysis only the results obtained from 62 male and 41 female infants who had remained quiet throughout the procedure were used. The average difference between the highest and lowest of the 6 readings obtained was 9·8 mm. Hg, the largest individual difference being 34 mm. Hg. No statistically significant difference in systolic blood pressure between males and females could be demonstrated, nor between the upper and lower limb.

The authors consider the wide variability of the results to be inherent in the method, but the variation observed between readings from different patients was greater than that between the three readings from one limb in individual patients. They regard the method as satisfactory provided its limitations are recognized, and they recommend that a minimum of three, and preferably five, readings should be made and the results of these averaged. *H. G. Farquhar*

263. **Changes in the Clinical Picture and in the Treatment of Suppurative Pneumonia in Childhood.** (Wandlungen im Erscheinungsbild und in der Therapie der kindlichen abszedierenden Pneumonie)
L. WEINGÄRTNER. *Monatsschrift für Kinderheilkunde* [*Mschr. Kinderheilk.*] **103**, 1–8, Jan., 1955. 12 figs., 11 refs.

Grouping together all cases of primary lung abscess, secondary staphylococcal pneumonia, metastatic lung abscess, and secondary lung abscess under the collective title of " suppurative pneumonia " the author reviews 405 such cases seen at the University Paediatric Clinic, Leipzig, between 1944 and 1953. Individual case histories illustrating the 4 different types of lesion are given, together with an account of the changes which have been observed in the clinical course since the use of antibiotics became possible. At this clinic lung aspiration to determine the nature of the infecting organism is common practice and intrapleural antibiotic treatment has been found very effective.

The cases of primary abscess occurred mainly in young infants (of which 20% were premature), and among 134 such cases, 34 of the patients developed pyopneumothorax, from which 11 died; in the fatal cases the course was rapid, and if the response to antibiotics was not almost immediate these drugs appeared to have little effect. There were 204 cases of secondary staphylococcal pneumonia, which developed in most cases as a complication of the infectious fevers and bronchopneumonia; the majority of these cases occurred in older children and here the prognosis was more favourable. In the small group of cases of metastatic lung abscess the lesion was associated with sepsis of the umbilicus and skin, otitis media, and osteomyelitis; before the advent of antibiotics this group carried the worst prognosis, but in recent years the availability of these drugs has brought considerable improvement. The cases of single lung abscess, for which treatment by surgical drainage is advised, were considered to be mostly due to inhalation of a foreign body or to a blood-borne infection. In conclusion a comparison is made between the present series of cases and a similar series seen at the

same clinic in the period 1924–39. The most notable differences were in the age of patients affected, the type of causal organisms, and of course the results achieved with antibiotics. *David Morris*

264. **Five Cases of Acute Infective Polyneuritis (Guillain–Barré Syndrome) in Children**
P. AYLETT. *Archives of Disease in Childhood* [*Arch. Dis. Childh.*] **29**, 531–536, Dec., 1954. 37 refs.

265. **Purulent Meningitis in the Newborn.** (Les méningites purulentes du nouveau-né)
R. DEBRÉ, P. MOZZICONACCI, and M. BERKMAN. *Semaine des hôpitaux de Paris* [*Sem. Hôp Paris*] **30**, 4479–4492, Dec. 22, 1954. 42 refs.

Purulent meningitis is uncommon in infants less than one month old, only 131 cases having been reported in the literature up to 1943. The present authors discuss 13 such cases encountered between 1946 and 1953 at the Hôpital des Enfants-Malades and one other centre in Paris, together with 33 other cases reported in the literature during the same period. The responsible organism in more than half of these 46 cases was of the intestinal group (*Bacterium* (*Escherichia*) *coli* greatly preponderating), which is in contrast to the findings in meningitis in older babies.

A long or complicated labour had preceded the birth of many of these patients, 8 of whom were twins and 7 premature infants. Clinical evidence of meningeal infection was scanty: the temperature was elevated briefly or not at all, but refusal of feeds, with consequent loss of weight, and unexplained cyanosis were frequently noted. Some of the infants were lethargic and unresponsive, whereas others cried without cessation. Convulsions—local rather than general—occurred in 10 cases, and repeated vomiting was another suggestive symptom. Physical signs could not be relied upon, neck rigidity occurring seldom, though sometimes some nuchal hypotonicity was observed. In a minority of cases some increased tension of the fontanelle was noted. Other signs encountered were a general muscular flaccidity and ocular palsies or nystagmus; occasionally there were signs referable to infection elsewhere in the body. When the site of the disorder was recognized the principal diagnostic difficulty was in distinguishing meningitis from intracranial haemorrhage. The signs and symptoms of the latter, however, are often more violent, with generalized convulsions, bulging fontanelle, and shock, while a symptomless interval after birth is in favour of meningitis. But it is emphasized that the two conditions may coexist or succeed one another, and that a blood-stained cerebrospinal fluid (C.S.F.) must not be assumed to be sterile.

The authors advocate the performance of an early diagnostic lumbar puncture whenever there are unexplained symptoms in a newborn infant; if the fluid obtained is not clear, streptomycin should be given intrathecally and chloramphenicol by mouth without waiting for the results of culture, this combination of drugs having been found most efficacious in meningitis due to intestinal organisms. They draw attention, however, to the physiological xanthochromia frequently found in neonatal C.S.F., and accept a wider range of normality for the cell count and protein content of such fluid. The mortality in meningitis due to organisms of the intestinal group remains high, 12 out of 24 cases in this series proving fatal. In pneumococcal meningitis the prognosis is better, all 7 patients surviving; in the 2 cases treated by the authors intrathecal streptokinase was given, in spite of the risk of side-effects, to prevent spinal block. As might be expected, the prognosis for meningococcal meningitis in this age group is good, recovery occurring in all 6 cases in this series, 3 of them without intrathecal treatment. In the series as a whole the mortality was 34% (15 deaths), with neurological sequelae in 6% (3) of the survivors.

The article concludes with a discussion of the possible routes of infection, examples being given of cases in which antepartum or intrapartum transmission was probable or certain, although in most cases the infection is contracted after birth. A plea is made for the administration of prophylactic chemotherapy to both mother and child after prolonged or complicated deliveries.
M. E. MacGregor

266. **A Clinical Study of 100 Cases of Purulent Meningitis in Infancy.** (Étude clinique de cent cas de méningites purulentes du nourrisson)
P. MOZZICONACCI and M. BERKMAN. *Semaine des hôpitaux de Paris* [*Sem. Hôp. Paris*] **30**, 4492–4504, Dec. 22, 1954. 2 figs.

A study is presented of 100 cases of purulent meningitis in babies between the ages of one month and 2 years, encountered between 1946 and 1953 at the Hôpital des Enfants-Malades, Paris. The maximum incidence was in the first few months of life, infections with organisms of intestinal origin, such as *Bacterium* (*Escherichia*) *coli*, being confined to the very young. The meningococcus was the agent most frequently responsible, accounting for 46 cases. Pneumococci and *Haemophilus influenzae* accounted for 17 and 13 cases respectively. In 10 cases the organism was not identified. Meningococcal infection was commonest in winter, and pneumococcal meningitis in spring. The portal of entry of the infection was seldom evident.

The most constant clinical sign was fever, followed in order of frequency by restlessness and crying, vomiting, neck rigidity, impairment of consciousness, and increased tension of the fontanelle. Convulsions, purpura, loss of muscle tone, diarrhoea, and ocular and limb palsies were occasional findings. Attention is drawn to the fact that absence of fever, of neck rigidity, and of increased tension of the fontanelle in no way rules out the diagnosis of meningitis in an infant.

In general, three main forms of presentation could be distinguished: (1) with neurological signs, which was the most usual, (2) with predominant gastrointestinal symptoms, and (3) with signs of a generalized infection.

In 39 cases the condition was misdiagnosed on admission to hospital, being most commonly attributed to otitis media or gastroenteritis; in 9 of these a coexisting infection was correctly diagnosed, but the meningitis was overlooked. The importance of an early diagnostic

lumbar puncture in any case of unexplained illness or fever in a baby is emphasized, though in 7 cases in this series the cerebrospinal fluid (C.S.F.) withdrawn at first was normal or contained only an excess of lymphocytes. On discovery of a purulent C.S.F. treatment was started immediately, as a routine, with intrathecal streptomycin, followed by oral chloramphenicol and sulphonamide and intramuscular penicillin. Subsequent treatment was dictated by the nature and sensitivity of the organism isolated. In 44 cases subdural or ventricular puncture was required, in 20 of these via a cranial burr-hole. Subdural collections of sterile fluid were observed in 9 cases and treated by single or repeated aspirations. In 5 cases of pneumococcal origin streptokinase was given by the intrathecal route. The occurrence of convulsions, coma, or "toxicosis" worsened the prognosis considerably, while delay in diagnosis, often the consequence of indiscriminate chemotherapy before admission, was responsible for several deaths.

The results obtained are summarized as follows:

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Staphylococcus	2	1	—	1
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Unidentified	10	8	2	—
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The author considers that the psychological basis of the disorder is psychotic, not neurotic. She refers briefly to one patient, an asthmatic youth of 16, who had had eczema in infancy and who, when the asthma subsided, had to be admitted for a short period to a mental hospital. She adds that in her experience it is rare to find patients with eczema in mental hospitals, for once they have become frankly psychotic the eczema disappears.

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The homes of all these patients were visited, and in nearly all cases the mother was interviewed. Of the 84 patients with eczema, 6 had died from some infection during infancy—that is, before sulphonamides and antibiotics were available; the one death in the control group was accidental. Asthma, recurrent bronchitis, and seasonal rhinorrhoea were associated disorders in 57 of the patients with eczema, 30 having asthma alone; for the control group the comparable figures were 2 and 1 respectively. There had been one or more attacks of pneumonia in 17 of the eczema patients; none of the 57 controls had had pneumonia. In 19 patients the eczema had cleared up by the age of 3 years, but in over one-half it persisted to the age of 13. The authors state that since some of the patients were still under 20 at the time of follow-up it was not possible to arrive at an accurate estimate of the persistence rate at age 20, but there appeared to be "little tendency for the eczema to clear up in the teens". They also state that eczema appeared likely to persist longer in children with a family history of the condition and when the skin was greasier or drier than normal.

Elaine M. Osborne

Industrial Medicine

270. **Treatment of Lead Colic with Cortisone and Corticotropin**

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To estimate adrenal response to corticotrophin an eosinophil count is made before and after the first infusion. If there is a considerable fall in the number of eosinophils, then corticotrophin is the drug of choice, but if there is no marked decrease, then cortisone should be used. It is claimed that these steroids hasten recovery, promoting an earlier return of appetite and a feeling of health and well-being. *M. A. Dobbin Crawford*

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It is suggested that the routine of 5 days' treatment and 2 days' rest might with benefit be reversed, the drug being given for 2 or 3 days, with 5-day intervals. It is also suggested that a daily dosage of 2 g., or even 1 g., might well be given instead of the usual 3 to 4 g. daily. This would lessen the possible risk of depletion of trace minerals in the body. *M. A. Dobbin Crawford*

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Anaesthetics

273. The Effect of Blood Pressure Reduction with Arfonad on Renal Hemodynamics and the Excretion of Water and Electrolytes

J. H. MOYER, W. R. LIVESAY, and R. A. SEIBERT. *American Heart Journal* [*Amer. Heart J.*] **48**, 817–825, Dec., 1954. 6 refs.

The effect of reducing the blood pressure with "arfonad" on renal haemodynamics and on the excretion of water and electrolytes was studied by the authors at Baylor University College of Medicine, Houston, Texas, on 9 subjects with normal blood pressure. The subjects lay supine and were unanaesthetized; blood pressure was measured by intra-arterial manometry, the glomerular filtration rate with inulin, renal plasma flow with PAH, and urinary sodium and potassium with a Beckman flame photometer. After three successive 10-minute control periods, arfonad was given intravenously dissolved in 5% glucose in water at the rate of 2 to 4 ml. per minute. With rapid infusion the fall of blood pressure was precipitous, causing nausea and vomiting in 4 subjects, urticaria in 2, and itching in one. When, however, the blood pressure was gradually reduced over 10 to 20 minutes the side-effects were much less. Observations were made during three 10-minute periods in the first half-hour, during two 10-minute periods after one hour, and also after 2 hours. In 8 of the subjects, while the effects of arfonad were still present, an infusion of noradrenaline was given to restore the blood pressure and three successive 10-minute samples were collected.

All the subjects developed hypotension, which was maximal after 2 hours when arfonad was infused at a rate of 10 mg. per minute. There was a sharp diminution in renal blood flow, with a parallel reduction in glomerular filtration rate, water and sodium excretion, and an initial diminution in potassium excretion. There was an insignificant rise in peripheral vascular resistance, and increase in the pulse rate was not marked.

After the experiment, as the blood pressure returned to or above control values, glomerular filtration rate, renal blood flow, and excretion of water and sodium all rose, but not to control values; potassium excretion on the other hand often exceeded control levels. These findings suggest that glomerular filtration rate was reduced without impairment of tubular reabsorption, so that the percentage reabsorption of water and sodium was greater although the absolute amounts were less. The authors suggest that this point must be considered in administering fluids during surgical procedures performed under controlled hypotension. It is pointed out that since a return of renal function towards normal occurred on administration of noradrenaline, even while the effect of arfonad was continued, the depression of this function must have been due to the hypotension and not specifically to the arfonad. *B. L. Finer*

274. Physiological Principles in the Treatment of the Unconscious Patient

W. W. MUSHIN. *British Medical Journal* [*Brit. med. J.*] **1**, 1116–1119, May 7, 1955. 1 fig.

275. Importance of the Perineural Spaces in Nerve Blocking

D. C. MOORE, R. F. HAIN, A. WARD, and L. D. BRIDENBAUGH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **156**, 1050–1053, Nov. 13, 1954. 1 fig., 17 refs.

In reviewing 2 deaths and 11 cases of transverse myelitis following the paravertebral injection of "efocaine" at the Mason Clinic (University of Washington School of Medicine), Seattle, it was noted that the distance of the injection site from the intervertebral foramen in one case was 8 cm. by post-mortem measurement, while in 9 others the intercostal nerves had been injected under direct vision at thoracotomy. It seemed unlikely, therefore, that in these cases the drug had been injected inadvertently into an outward prolongation of the subarachnoid space, which is the explanation usually given of such sequelae. Anatomically, the pia mater is continuous with the epineurium of the peripheral nerves; therefore there is a possibility that fluid injected intraneurally may spread centrally via the perineural spaces and thus reach the spinal cord through the intervertebral foramina.

When efocaine was injected intraneurally into 26 of the exposed lumbar nerves of 11 monkeys under pentobarbitone anaesthesia at a point 3 to 4 cm. from the intervertebral foramina, 2 monkeys developed respiratory paralysis during the course of the operation and died, the procaine concentration in the cerebrospinal fluid of one being 58 mg. per 100 ml.; it was not determined in the other fatal case. Among the survivors the procaine concentration of the spinal fluid varied from 0·2 to 58 mg. per 100 ml. One monkey developed a transverse myelitis and 6 paralysis of a leg. The ease with which the intraneural injection could be made varied (apparently with the location of the needle tip within the nerve) and the concentration of procaine in the spinal fluid and the severity of the clinical effects were inversely proportional to the resistance encountered.

The authors conclude that efocaine, and possibly other substances, can be introduced into the cerebrospinal fluid and spinal cord by direct injection into the nerves distal to the intervertebral foramina.

A. M. Hutton

276. Renal Function during Controlled Hypotension with Hexamethonium and following Norepinephrine

J. H. MOYER, G. MORRIS, and R. A. SEIBERT. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **100**, 27–32, Jan., 1955. 4 figs., 2 refs.

Radiology

RADIOTHERAPY

277. **Radiotherapy of Cushing's Syndrome**
J. F. P. SKRIMSHIRE. *Lancet* [*Lancet*] **1**, 270–272, Feb. 5, 1955. 1 fig., 8 refs.

Cushing's syndrome may be due to an adrenocortical tumour or to hyperplasia resulting from increased pituitary adrenocorticotrophic activity. When no tumour is found on exploration of the adrenal glands, the amount of cortical tissue may be reduced surgically or its activity may be diminished by irradiation of the pituitary gland. Bilateral adrenalectomy produces an excellent remission of symptoms, but it is a severe operation and necessitates substitution treatment with cortisone. Irradiation of the pituitary gland, on the other hand, which produces considerable improvement in suitable patients, is simple, involves no operation risk, and is not followed by chronic adrenal insufficiency. If a cortical tumour can be excluded, therefore, radiotherapy should be used as the initial treatment; if it fails, surgery can still be undertaken later.

The present author reports the treatment at St. Thomas's Hospital, London, of 6 patients, all females between 19 and 36 years of age. The clinical diagnosis of Cushing's syndrome was confirmed by urinary corticosteroid and 17-ketosteroid estimations. Virilism and increased androgen excretion, which would have suggested an adrenal cortical tumour, were not observed. Deep *x*-ray therapy was given to the pituitary fossa with a high-voltage unit (250 kV peak, H.V.L. 1·75 mm. Cu) by six ports. A maximum dose of 4,000 to 5,000 r was given in 28 to 30 days. The only supplementary treatment consisted in a reducing diet to control obesity.

In assessing progress the following factors were studied: (1) general appearance; (2) texture of skin, striae; (3) menstrual history; (4) urinary steroid excretion; (5) glucose tolerance; and (6) blood pressure. One patient died of cerebral haemorrhage associated with long-standing hypertension 5 months after treatment. In 4 out of the 5 survivors there was considerable improvement, the fifth showing only slight improvement which has, however, been maintained for 3 years. Plethora began to diminish within 1 to 3 months of treatment, and the polycythaemia present in 2 cases disappeared during the same period. Hirsuties was uninfluenced, but menstruation was reestablished in all cases, though it ceased again in one and became irregular in 2. Glucose tolerance improved in all cases and corticosteroid excretion fell in 4, but that of 17-ketosteroids was reduced in only 2 cases. The blood pressure was reduced in all cases, but in only 2 did it become normal.

The diagnosis of Cushing's syndrome and the differentiation of the two types are discussed. In cases due to an adrenocortical tumour the history tends to be short and sexual changes are prominent, whereas cortical hyperplasia is most often associated with a long history, prominent metabolic disturbances, and little virilism. The prognosis in untreated cases is poor, death occurring in 50% within 5 years of diagnosis. Although spontaneous variations in activity may occur, the morbidity in those patients who survive longer is high. While the complete removal of one adrenal gland and nine-tenths of the other is as logical a form of treatment in cases of cortical hyperplasia as subtotal thyroidectomy for thyrotoxicosis, the author considers controlled Cushing's syndrome to be a preferable state to controlled adrenal insufficiency and therefore advises radiotherapy in the first place. If the progress of the disease is not arrested within 6 to 12 months, surgery can be undertaken with undiminished chances of success. *I. G. Williams*

278. **The Rationale and Results of Simple Mastectomy plus Radiotherapy in Primary Cancer of the Breast**
L. H. GARLAND. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **72**, 923–941, Dec., 1954. 5 figs., bibliography.

" The problem of cancer of the breast is fundamentally the problem of cancer outside the breast." When spread has occurred outside the breast, radical mastectomy can cure only those cases in which the disease is still confined to the removable tissues—about 10% of all cases when first seen—and may penalize as many cases as it saves if the dissection spreads cancer emboli via the lymphatic and blood vessels to other sites. Moreover, owing to the difficulty of determining the true degree of spread operative treatment is undertaken in many cases which are beyond its scope. In such cases simple mastectomy would be as effective in terms of survival as radical mastectomy and is a safer and less mutilating operation. In addition, radical mastectomy is followed by oedema of the arm in 5 to 10% of cases and weakness of the arm in 10%, whereas such complications are rare after the simple operation. Simple mastectomy followed by vigorous irradiation has been advocated in all operable cases of carcinoma of the breast, particularly by McWhirter, who reports an absolute 5-year survival rate of 42% compared with about 34% for radical mastectomy in most published series. The status of the axillary lymph nodes is regarded as of no importance in planning or executing treatment according to this programme.

A study of the results reported in the literature shows that the 5- and 10-year survival rates in properly selected operable cases of carcinoma of the breast are essentially the same whether the treatment be radical mastectomy or simple mastectomy with postoperative radiotherapy. In these circumstances most women, if given the choice, would probably prefer the simple operation. The radical operation is still to be preferred for the obese, the tuberculous, or the unstable patient who will not cooperate

to complete her radiotherapy, while simple mastectomy should not be undertaken unless expert postoperative radiotherapy is available. *I. G. Williams*

279. *X*-ray Treatment of Ankylosing Spondylitis

G. HILTON. *Rheumatism* [*Rheumatism*] **11**, 10–15, Jan., 1955. 4 figs., 1 ref.

Writing from University College Hospital, London, the author states that the treatment of ankylosing spondylitis by immobilization or physiotherapy alone has proved of only temporary value, therapy with vaccines and gold has failed, and cortisone, while useful in an acute phase, has not proved curative. Radiotherapy, however, has changed the whole outlook. The earlier the treatment —preferably when still only the sacro-iliac joints are involved—the better the results. Misdiagnosis of an abnormal radiological picture—for example, one of osteitis condensans ilii—is a possible cause of failure.

In the acute phase, when there is general illness, complete rest is indicated and irradiation at this stage is contraindicated. Later, however, even advanced cases can be benefited by localized radiation. It is important to consider the dosage received by the gonads. In the male the dose to the testes, if adequately protected, is negligible (about 5 r), and libido is not affected by such a dose, although it is often impaired by the general effects of the disease; sperm counts made before and after treatment have shown no reduction in numbers. In the female, however, the situation is very different and it is impossible completely to avoid affecting the ovaries. A direct sacro-iliac field will give an ovarian dose of 400 to 500 r; this will always cause amenorrhoea, which may be permanent in women approaching the menopause, and may last 8 to 12 months in younger women. A later pregnancy may produce a normal child, and genetic damage may not show itself until the second or even third generation; hence some authorities advise a full sterilizing dose of radiation for all female patients. In the author's view irradiation should be given to younger women only when there are definite radiological changes or physical incapacity. Before beginning treatment septic foci and anaemia should be dealt with. The haemoglobin level does not usually fall during treatment, and may even rise. The number of leucocytes should be checked by making weekly counts, treatment being suspended if the count falls. A radiograph of the chest should always be taken, for irradiation may stir up a latent focus of tuberculosis.

The aim in treatment of spondylitis is quite different from that in cancer therapy and much smaller doses are needed; the beneficial effects are probably due to depression of cell activity, increased blood and lymph flow, diapedesis, and proliferation of fibroblasts. In technique, wide-field *x*-ray "baths" have been generally abandoned, and irradiation is now given to the sacro-iliac joints plus the lumbar spine or whole spine—preferably the whole spine, to lessen the chances of recurrence —200 to 250 kV being used for the spine and large joints, and 120 to 150 kV for small joints and muscle attachments. Three spinal fields 8 cm. wide and 15 to 20 cm. long are used. In the male the sacro-iliac joints are treated by one transverse field, but in the female each side is treated by a separate tangential field in order to minimize dosage to the ovaries. There is no general agreement on optimum dosage; a usual course is a total surface dose of 1,500 to 2,000 r, 300 r being given to one field or 200 r to 2 fields daily and the whole treatment spread over one month. For peripheral joints a total of 1,000 r is delivered to the centre of the joint over 2 weeks. Physiotherapy, consisting first in passive and then in active movement, should be given concurrently, and breathing exercises to improve chest expansion are most important. Surgery, such as osteotomy of the hip-joint or spine, is of very little value and may entail the risk of causing increased ossification, while manipulation only aggravates the condition.

The results of treatment depend largely on the stage of the disease at which irradiation is begun. In early cases in which only the sacro-iliac joints are involved signs and symptoms may disappear in 100% of cases. In moderately advanced cases this can be expected in about 70%, but even bedridden patients can be greatly helped and become useful citizens. Involvement of the hip-joints causes the most crippling disablement and has the worst prognosis. Complete relief of pain may take 1 to 3 months to achieve. There is no close correlation between the erythrocyte sedimentation rate (E.S.R.) and activity of the disease; a fall in the E.S.R. may lag months behind clinical improvement, and treatment policy should therefore be guided primarily by symptoms. In such a chronic disease it is difficult to say whether cure can be permanent, since the data are as yet inadequate, but the author has known cases in which the progress of the disease was halted for 10 to 15 years. Recurrences may be due to incomplete spinal treatment, unsuitable occupation, exposure, or severe illness of other sorts. Treatment has little influence on the radiological picture, and calcification or ossification usually remains unchanged. Rehabilitation, after-care, and the choice of work are most important; both heavy manual work and a wholly sedentary occupation are to be avoided. *J. Walter*

280. Treatment of Papilloma of Bladder with Radioactive Colloidal Gold Au^{198}

F. ELLIS and R. OLIVER. *British Medical Journal* [*Brit. med. J.*] **1**, 136–139, Jan. 15, 1955. 4 figs., 7 refs.

The difficulty of distinguishing between benign and malignant papillomata of the bladder is stressed, and the unsatisfactory results obtained in the treatment of these lesions with cystodiathermy, total cystectomy, *x*-irradiation, and an intravesical balloon containing a radioactive solution are discussed. At the Churchill Hospital, Oxford, it was decided to explore the possibility of using the β radiation of radioactive colloidal gold (^{198}Au). The β emission of ^{198}Au has a range in tissue of about 0·3 mm., which is roughly the thickness of the average papilloma.

Careful preliminary tests showed that the colloid was not precipitated on the bladder wall or absorbed by the blood or lymph. It was therefore decided to try this treatment on a 67-year-old man with multiple bladder

papillomata, 300 mc. of ^{198}Au in 100 ml. being taken into a special syringe and injected through a Foley catheter into the bladder. The balloon of the Foley catheter was inflated with 5 ml. of fluid and used to seal the neck of the bladder. After 2½ hours the bladder was drained and rinsed, and the fluid and the urine collected over the next 24 hours were kept for measurement of activity. The dose received by the bladder epithelium was estimated to be 3,000 r. After 2 months a further dose of 2,400 r was given by the same method. At cystoscopy 6 weeks later only a small ring of papillomata was seen round the neck of the bladder where the Foley balloon had protected the epithelium. This small area was then treated locally with radioactive cobalt. At cystoscopy 15 months after the last treatment the bladder appeared normal. The clinical features of this case are described in detail.

The authors' recommended routine procedure and the special protective gun which has been made to enclose a 100-ml. syringe are described. Although this method of treatment was designed initially for the treatment of multiple villous papillomata, it has been found suitable, in conjunction with other methods, for the treatment of papillomatosis with carcinoma and for decreasing the surface activity of a malignant growth before a more radical technique is employed. The authors state that theoretically it should also be possible to treat papillomata of the pelvis of the kidney by this method. This procedure, provided it is accurately carried out, is safe for both patients and staff. Altogether 22 patients have been treated without any untoward effects.

[This paper should be read in the original by those interested in the subject.] *R. D. S. Rhys-Lewis*

RADIODIAGNOSIS

281. **Diagnosis of Tumours of the Glomus Jugulare**
S. HOLESH. *Lancet* [*Lancet*] **1**, 169–170, Jan. 22, 1955. 3 figs., 25 refs.

On the basis of 5 cases in which the diagnosis of tumour of the glomus jugulare was made at the Westminster Hospital, London, with histological confirmation in 2 of them, the author discusses the clinical and radiological features of this condition, which is being reported with increasing frequency. The tumour may arise either in the adventitia of the jugular bulb or from a glomus body within the temporal bone, and its histology resembles that of a carotid-body paraganglioma. It may spread by progressive expansion of the middle ear, bulging the drum and eventually protruding into the external canal as a granular mass or polyp. Alternatively extension may occur medially along the petrous pyramid with eventual invasion of the cranial cavity. Except in children, however, the tumour grows very slowly, the duration of symptoms varying from 9 months to 20 years. Malignancy supervenes after a long benign course in 15 to 20% of cases. The commonest symptoms are chronic otorrhoea, progressive deafness, tinnitus, and haemorrhage from the affected ear. A bruit may occasionally be heard over the mastoid area and neck. As the tumour spreads multiple cranial palsies characteristically develop, involving usually the 5th to the 12th cranial nerves.

The radiological features are: (1) sclerosis of the mastoid process; (2) destruction of the *lower* portion of the petrous pyramid, leaving the ridge as an intact shell; (3) enlargement of the jugular foramen, with perhaps a mass in the posterior nasopharynx; (4) on arteriography, a tortuous mass of new vessels in the petro-temporal region or posterior fossa; and (5) signs of raised intracranial pressure when the tumour has extended widely into the middle or posterior fossa. Tomography of the petrous bone in the antero-posterior projection is the most useful procedure for demonstrating the characteristic area of bone destruction. The differential diagnosis includes acoustic neuroma, primary tumour of the nasopharynx, chordoma, and metastatic carcinoma.

G. Ansell

282. **The Roentgenographic Diagnosis of the Arnold–Chiari Malformation**
R. SHAPIRO and F. ROBINSON. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine* [*Amer. J. Roentgenol.*] **73**, 390–395, March, 1955. 3 figs., 10 refs.

283. **Demonstration of the Pericardial Shadow on the Routine Chest Roentgenogram: a New Roentgen Finding. Preliminary Report**
V. KREMENS. *Radiology* [*Radiology*] **64**, 72–80, Jan., 1955. 10 figs., 4 refs.

The author of this paper from the Albert Einstein Medical Center, Philadelphia, draws attention to the possibility of visualizing the pericardium along the left border of the heart. The outline of the pericardium, normal or abnormal, can be seen in those cases in which the underlying epicardial fat appears as a translucent zone. In necropsy specimens there is considerable variation in the amount of adipose tissue present, depending, in part, on the general nutritional status of the patient before death; this adipose tissue is encountered except when death follows a chronic wasting illness. It is best visualized on the routine postero-anterior chest radiograph with not more than one-tenth of a second exposure and a fine-focus tube at 6 feet (1·8 m.). The author has not found oblique projections of any help, but use of a Bucky diaphragm has resulted, in some cases, in better delineation of the pericardial shadow. Where the pericardium appears thickened, tomograms obtained in the prone position with the tube centred on the left border of the heart and cuts at 2 to 6 cm. may be very helpful. The epicardial fat appears as a curvilinear shadow up to 2 mm. in width; it is best seen along the left ventricular border and also in the pulmonary-artery segment, although in the latter area overlying lung shadows may be very confusing. The pericardial shadow, thrown into relief by the subjacent translucent epicardial fat, is normally represented by a curvilinear shadow of similar density to the heart shadow. It is of constant width, up to 1 to 2 mm.

The author has not yet visualized this pericardial shadow in a sufficient number of cases to be able to

determine its incidence, but he believes it is demonstrable in not more than 5% of healthy subjects. It is less frequently seen in the older age group. A pericardial shadow more than 2 mm. in width must indicate either current or previous pericardial thickening.

John H. L. Conway-Hughes

284. **Unsolved Problems in the Radiological Diagnosis of Peptic Ulcer. The Atropine Test.** (Ungelöste Probleme der Röntgendiagnostik des peptischen Geschwürs. Die Atropinprobe)
E. Ötvös. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **81**, 749–757, Dec., 1954. 2 figs., 13 refs.

Even with the most expertly applied radiological technique the diagnosis of a duodenal or gastric ulcer may still remain uncertain. In this paper from the Third Municipal Polyclinic, Budapest, the author contends that the diagnosis can be made certain by means of an atropine test devised by himself. The procedure for this is as follows. A day or two after the routine *x*-ray examination the patient is given a subcutaneous injection of 1 mg. of atropine sulphate, a barium meal is given 30 minutes later, and the emptying of the stomach is observed on the screen. The result of the test is manifest after 2 hours, and is stated to depend on the fact that emptying of the normal stomach is not influenced by the atropine injection, but in the presence of an intramural gastric or duodenal inflammatory condition the atropine produces a definite dyskinesia, whereby in spite of good or even excessive peristalsis a residue of the barium, often quite appreciable, remains in the stomach for up to 2 hours after the meal. The author has found that without the atropine the same stomach showed a normal emptying time. This behaviour of the stomach is claimed to be typical of the intramural inflammation which almost invariably accompanies a chronic ulcer. A negative response to the atropine test in the presence of radiographic evidence of ulceration points to an acute, superficial ulcer.

A. Orley

285. **Observations on Cholecystography with "Biligrafin" and Its Diagnostic Implications.** (Beobachtungen bei Cholezystographien mit Biligrafin und die sich daraus ergebenden diagnostischen Folgerungen)
F. E. Stieve. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Rontgenstr.*] **81**, 735–748, Dec., 1954. 9 figs., bibliography.

The demonstration of the biliary passages by the intravenous injection of "biligrafin" does not depend on concentration of the bile in the gall-bladder, as is the case in ordinary cholecystography. But, as the author points out in this communication from the University Roentgenological Institute, Munich, such a concentration may occur also with biligrafin, in which case opacification of the gall-bladder may appear in the form of layers of varying density. These layers eventually disappear slowly by diffusion.

From a study of 257 cholecystograms the author claims to be able to distinguish "physiological" layering from that occurring in pathological conditions. A dense biligrafin shadow may mask a stone, which may become apparent only with maximal contractions of the gall-bladder. Similarly, when there are two layers of different density in the gall-bladder—a dense layer above a transparent one—the upper layer may mask a floating stone. In the author's experience the relative indications for cholecystography with biligrafin are as follows: (1) when the gall-bladder cannot be visualized by means of the usual contrast media; (2) when an intestinal disease prevents absorption of the medium; (3) when there is reason to suspect excessive excitability of the gall-bladder; (4) when the patient cannot take the contrast medium by mouth; and (5) when a diagnosis is urgently required.

A. Orley

286. **Postcholecystectomy Oral Cholangiography**
J. R. Twiss, L. Gillette, S. L. Beranbaum, M. H. Poppel, and E. C. Hanssen. *Archives of Internal Medicine* [*Arch. intern. Med.*] **95**, 59–65, Jan., 1955. 9 figs., 22 refs.

The authors have already described their technique for rendering the biliary ducts visible (*Amer. J. med. Sci.*, 1954, **227**, 372; *Abstracts of World Medicine*, 1954, **16**, 263), and in the present paper they discuss the cholangiograms obtained in 106 cases. This new method, in which the medium is given by mouth, yields results comparable to those obtained when "biligrafin" is administered intravenously. A double dose of "telepaque" (iopanoic acid) is given after a 12-hour fast, and 2 hours later 2 drachms (7 ml.) of camphorated tincture of opium (paregoric) is administered. At 5 or 14 hours after the medium has been given—both are optimum points—radiographs are taken of the liver and duct areas, and these are repeated at hourly intervals for 3 or 4 hours. When adequate radiographs have been obtained the patient either inhales amyl nitrite or takes a fatty meal, and a further radiograph is taken 30 minutes later.

Radiographs of diagnostic quality were obtained in cases in which there was no shadow after conventional cholecystography and also in patients whose gall-bladder had been removed. In a control series of 42 patients without symptoms after cholecystectomy the authors found that a non-progressive slight dilatation of the common bile duct was general. By this method cholangiograms were obtained in 32 cases of dyskinesia, in which the incidence of duct dilatation was found to be significantly greater than in controls; in 6 cases of cystic-duct remnant, all of which showed the lesion; in 2 of retained gall-bladder remnant or "re-formed" gall-bladder; in 3 of stone in the duct; and in 6 cases of non-functioning gall-bladder, in 3 of which the gall-bladder was demonstrated although no shadow had been observed with earlier conventional cholecystography; stones were seen in 2 of this last group of cases.

The bile ducts were visualized in 76 of the 106 cases. Of 36 comparable cases in which biligrafin was given intravenously, the ducts were demonstrated in 30.

A. M. Rackow

See also Tuberculosis, Abstract 57, and Cardiovascular System, Abstract 128.

History of Medicine

287. **Child Care in Ancient Greece.** (La puériculture dans l'antiquité Grecque)
S. BARTSOCAS. *Archives françaises de pédiatrie* [*Arch. franç. Pédiat.*] **12**, 71–83, 1955. 6 figs.

In this contribution from the Evangelismos Hospital, Athens, the author deals with certain aspects of neonatal and infant care as described in the writings of the best known of the ancient Greek, as well as Roman and Byzantine, medical writers [so that the title of the paper is not strictly accurate].

The author points out that although child care was not very advanced in the Hellenic era, nevertheless many progressive ideas were then current. Once the belief was overcome that everything and everyone who touched a woman in childbirth was unclean, midwives and wet-nurses were available to look after mother and child, and therefore codes of behaviour and requirements for their duties were compiled and are here described. Regarding breast-feeding, it is interesting to note that during the period of decline of Hellenic supremacy mothers had to be reminded that their duty lay in breast-feeding their children themselves.

Discussing the care of the infant itself, the author describes the ancient views on the causes and management of crying, the problem of weaning, and methods of social education. From some of the extracts given it is clear the Greek physicians had already begun to grasp some of the rudiments of hygiene, in that they deprecated the habit, then prevalent, of mothers and wet-nurses premasticating the food for the infant. The author also cites a number of extracts discussing the problem of sleep, which preoccupied Plato, Aristotle, and Galen, and mentions the conflicting views on the swaddling of infants.

[This is an interesting paper, which should be consulted for further details.] *P. I. Reed*

288. **Christopher Merrett, F.R.C.P. (1614–1695), First Harveian Librarian**
C. DODDS. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **47**, 1053–1056, Dec., 1954. 11 refs.

The years of Christopher Merrett's life (1614–1695) not only saw the foundation of the Royal Society and the recognition of the experimental method in science, but it witnessed a revolution in the outlook of medicine with Harvey's discovery of the circulation of the blood. During this period also the Royal College of Physicians, which was founded in 1518, reached a critical stage in its history. Its work consisted wholly in the examination of the credentials of those claiming to have medical knowledge and the issue of licences to practise. In 1614 the College moved from its original headquarters in Linacre's house to new premises at Amen Corner, where more accommodation was available for the growing library. The keen interest of Harvey himself resulted in further development of the library. He drew up the first rules in 1632, and, it is generally assumed, provided an extension which was opened in 1653. In 1656 he established a trust fund for the maintenance of a permanent official who was to be keeper of the library, reside in the College, and receive £20 a year after Harvey's death. Merrett, a close friend of Harvey and already resident keeper, continued as the first Harveian Librarian, though his formal appointment is not recorded. Under his guidance the library increased greatly in size; many gifts were received, including a generous donation in 1665 from the Marquess of Dorchester. A complete catalogue which was prepared by Merrett in 1660 is still in existence.

Merrett was educated at Gloucester Hall, Oxford. He developed a considerable private practice in London, and became a Fellow of the Royal College of Physicians in 1651. He was a Censor seven times between 1657 and 1670 and an Elect of the College. His scientific interests were wide, and in the first official record of the Royal Society Merrett's name appears as a founder member. The first change in his fortunes came with the Great Plague in 1665, when fear for his family made him desert the College for the country. In spite of Merrett's careful precautions thieves broke into the College in his absence and stole plate and money. Immediately after he returned to London, the Great Fire gutted the College; at the cost of his own possessions, which included a famous and extensive library, he saved some of the more important treasures and books, especially a complete set of the *Annals*. Nevertheless, he was blamed for the considerable losses, and antagonism grew steadily between Merrett and the College. In 1681 he was expelled for non-attendance at meetings, and after a legal action lasting two years he was ordered to restore College property still in his possession. He continued to attend meetings of the Royal Society, but his one attempt to regain his Fellowship of the College was dismissed, and little is known of his life thereafter.
F. M. Sutherland

289. **The Anatomical Drawings of Géricault (1791–1824).** (Les dessins d'anatomie de Géricault (1791–1824))
P. PIZON. *Presse médicale* [*Presse méd.*] **62**, 1855–1858, Dec. 25, 1954. 8 figs., 5 refs.

The library of the École Nationale Supérieure des Beaux-Arts, Paris, contains a collection of 34 anatomical studies by Géricault, of which 18 concern the anatomy of the horse and 16 are of the skeleton and muscles of man. The animal studies are in black and coloured crayon, the others in pen and ink wash. The drawings of the superficial architecture of the human body indicate a didactic rather than an artistic purpose, and this is

borne out by the marginal notes. Their homogeneity prove them to be contemporaneous. Experts, however, have shown that they are not original work but are copies of illustrations in two textbooks of anatomy for painters, which Géricault probably used in 1811 when he was 20 years old. There is evidence that at that period he devoted much time to copying classical art, in drawing from the living model, especially horses, and in teaching himself anatomy.

The story of the hunt for the originals is given in some detail [and provides a fascinating little study in artistic detection]. They were discovered partly by chance, but largely owing to the perspicacity of the finders. The two original sources were *Etude d'anatomie à l'usage des peintres* by Charles Monnet, published in Paris, and the *Anatomia per uso dei pittori e scultori* by Giuseppe del Medico, published at Rome in 1811, which itself owed much to the celebrated *Tabulae sceleti et musculorum corporis humani* of Albinus.

In a discussion of the artistic merits of Géricault's drawings the author points out that they have not the freedom of line and absolute mastery of Géricault's other and later works, such as the " Chasseur à cheval " (1812), the " Cuirassier blessé " (1814), and the collection of studies for " La course de chevaux libres ". Being largely copies, these drawings of 1811 are stilted in character and very different from his work of 1818–19, which was drawn from life and in which the exactness, keen observation, and faithfulness to nature for which he is famous are seen at their best, as in the dramatic " Les suppliciés ", and " Le rádeau de la Méduse ".

In 1820 Géricault visited England where he collected material for his " Grand Derby d'Epsom ", but returned to France already a sick man. In 1822 he sustained a severe injury to the spine in a fall from his horse and these injuries, which resulted in paravertebral and recurring abscesses, hastened his end. He died in January, 1824, at the early age of 33. *Thomas Marmion*

290. **Anton de Haën and the Beginning of Clinical Teaching in Vienna.** (Anton de Haën und der Beginn des klinischen Unterrichtes in Wien)
M. JANTSCH. *Wiener klinische Wochenschrift* [*Wien. klin. Wschr.*] **67**, 1–3, Jan. 7, 1955. 1 fig., 22 refs.

This paper from the Institute of the History of Medicine, University of Vienna, is a tribute on the 250th anniversary of his birth to Anton de Haën, who was one of the men who, during the 18th century, laid the foundations of the later renowned Viennese Medical School. De Haën (or de Haan) was born on December 8, 1704, at The Hague, studied in Leiden under Boerhaave, obtained his doctor's diploma in 1735 (a facsimile of the diploma with Boerhaave's signature is reproduced), and settled in practice in his native town.

In 1754 van Swieten, who at the request of the Empress Maria Theresa had undertaken the reform of the study of medicine at the University of Vienna, invited de Haën to come there as a teacher. De Haën accepted the invitation and brought to Vienna the methods of clinical teaching as they were practised in Leiden. De Haën was an enthusiastic teacher and was always interested in new methods, for example, in taking temperature with the thermometer then recently invented by Fahrenheit, and in correlating body temperature and pulse rate. Against the strong opposition of his colleagues he defended vaccination for smallpox. But the author stresses the fact that de Haën, in curious contrast to his progressive ideas as a teacher and as a medical practitioner, was greatly devoted to the study of magic and mysticism. He published two books on these subjects: *De magia liber* (1775) and *De miraculis liber* (1776), in which works he opposed the then current ideas of " enlightenment ". He died in Vienna in 1776. *A. Fessler*

291. **The Genius of Balzac from the Psychiatric Point of View (Genius and Madness).** (Le génie de Balzac du point de vue psychiatrique (génie et folie))
G. RAVIART. *Annales médico-psychologiques* [*Ann. méd.-psychol.*] **112**, 481–503, Nov., 1954. 2 figs.

292. **The Origin of the Morbid Physiology of the Circulation with Albrecht Haller's *Elementa physiologiae* (1756–60).** (Die Anfänge der pathologischen Physiologie auf dem Gebiet der Kreislaufforschung nach Albrecht Hallers *Elementa physiologiae* (1756–1760))
H. BUESS. *Gesnerus* [*Gesnerus* (*Aarau*)] **11**, 121–151, 1954. 12 refs.

293. **Cabanis and the Precision of Medical Science.** (Cabanis und die Gewissheit der Heilkunde)
E. LESKY. *Gesnerus* [*Gesnerus* (*Aarau*)] **11**, 152–182, 1954.

294. **" Diseases of the Heart and Aorta." By William Stokes (1854). A Modern Clinical Review**
R. MULCAHY. *Irish Journal of Medical Science* [*Irish J. med. Sci.*] **6**, 53–66, Feb., 1955.

295. **Thomas Hodgkin**
H. MORRISON. *New England Journal of Medicine* [*New Engl. J. Med.*] **251**, 946–948, Dec. 2, 1954. 2 figs., 4 refs.

296. **Nicolaus Steno.** [In English]
B. PEYER. *Gesnerus* [*Gesnerus* (*Aarau*)] **11**, 55–61, 1954.

297. **James Thomas Rudall, F.R.C.S. (1828–1907): His Life, and Journal for the Year 1858**
B. GANDEVIA. *Medical Journal of Australia* [*Med. J. Aust.*] **2**, 989–1008, Dec. 25, 1954. 4 figs., 21 refs.

298. **George Crabbe (1754–1832), Surgeon, Clergyman and Poet**
B. HILL. *Practitioner* [*Practitioner*] **173**, 712–716, Dec., 1954. 1 fig.

299. **Patrick Black (1813–1879). First " Administrator of Chloroform " at St. Bartholomew's Hospital, London**
J. L. THORNTON. *Anaesthesia* [*Anaesthesia*] **10**, 70–73, Jan., 1955. 2 figs., 4 refs.